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Studies on joint temperature, joint stiffness and muscle weakness in Rheumatoid Arthritis

An experimental and clinical investigation

BY

PER TISELIUS

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An experimental and clinical investigation

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av

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UPPSALA 1969

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INTRODUCTION

Rheumatoid arthritis (RA) shows a natural course with large variation in disease localization and disease intensity. The variation in the systemic as well as the local disease intensity (activity) makes a quantitation of symptoms and signs difficult and an evaluation of results of treatment often uncertain. The frequent lack of agreement between objective signs and patient's complaints adds to this uncertainty. For this reason, research interest has been focused mainly on objective or semi-objective methods for quantitation of disease activity and functional capacity. Such methods may relate to

(*a*) systemic disease activity (acute phase reactants, composite indices, e.g., Lansbury's Systemic Index),

(*b*) local disease activity in joints (synovial fluid examination of mucin clot formation, white blood cell count or viscosity, joint temperature determination, joint swelling by Jeweller's ring or water displacement),

(*c*) functional tests of the skeleto-muscular system (gripping strength, walking capacity, activities of daily living).

There is no answer to the question whether uniform agreement exists as to what criteria should be used. It very much depends upon which manifestation of the disease the examiner wants to evaluate during e.g., a specific programme of treatment. Tests for systemic disease activity do not appear to be suitable when following the results of physical therapy. Functional tests might indirectly reflect systemic disease activity but if they are sensitive enough for registration of less than very pronounced activity changes is not known. Composite indices are made up of different subjective and objective criteria and the use of them has been criticized by, e.g., Mainland (1967).

In this context it might be of interest to recapitulate some different clinical methods appearing in the literature that have been used to measure systemic as well as local disease activity in RA. In Table 1 a summary of the more common methods is given. As so many different criteria exist, it was found suitable to arrange them in four columns. In column 1 the patient's capacity in a test situation is given. Column 2 deals with so-called objective findings. Laboratory tests in this column are included in composite indices and therefore listed. The patient's interpretation of his symptoms is given in column 3 and the examiner's is listed in column 4.

Table 1. *Clinical methods for the assessment of inflammatory activity or functional capacity in patients with RA.*

Author	1 Patient's capacity	2 Objective findings	3 Patient's interpretation	4 Examiner's interpretation
Jansen (1930, 1931)			Tenderness	Stiffness, limitation of motion, swelling, bony deformity, crepitation, acute inflammation
Taylor (1937)		Radiological assessment	Pain, stiffness	Swelling, crepitation, limitation of movement, joint deformity
Bayles & Hall (1943)		ESR, Hb, weight	Pain, tenderness	Functional capacity, joint findings (swelling, warmth, redness, deformity)
Steinbrocker & Blazer (1946)		ESR, Hb, weight	Pain, tenderness, wellbeing	Joint swelling, joint motion, functional capacity
Holmdahl & Ingelmark (1946)		ESR, Hb, weight	Pain on motion, pain at rest	Employment status, functional capacity, joint findings (exudate, capsular thickening, restricted joint movement)
Steinbrocker, Traeger & Batterman (1949)		ESR, WBC, Hb, radiological assessment weight, fever	Weakness, tenderness, stiffness	Extra articular findings (nodules, tenovaginitis, iritis), joint findings (limitation of movement, swelling, effusion)
Horvath & Hollander (1949)		Joint heat by intra-articular temperature determinations		
Hart & Clark (1951)		Digital swelling by Jeweller's ring		
Joint commitee of the Medical Research Council and Nuffield Foundation (1954)	Functional tests (tying knots, ascending steps, walking time)			Limitation of movement
Empire Rheumatism Council (1955)		Radiological assessment ESR, Hb	Fitness, tenderness	Employment status, articular involvement in 68 joints (swelling, limitation of movement)
Mandel (1956)	Timing every day actions, walking time, grip power	ESR, Hb, weight	Pain at rest, lack of appetite, tenderness	Joint findings (swelling, warmth, range of motion), vasomotor imbalance, functional capacity

Lansbury (1956)	Grip power	ESR	Morning stiffness, fatigue, aspirin need, joint tenderness, pain on motion	
Shetlar *et al.* (1956)		Fever	Morning stiffness, sleep pattern, malaise, fatigability, weakness, appetite, joint pain	Joint findings (swelling, redness, heat) physical accomplishment
Smyth & Clark (1957)		Digital swelling by Jeweller's ring	Tenderness, pain on motion	Joint findings (heat, redness, effusion), joint circumference
Glyn (1958)	ADL functional tests	ESR, Hb, weight radiological assessment	Tenderness	Number of joints involved, limitation of movement
Savage (1958)	Grip power		Tenderness	
Cohen & Calkins (1958)	Grip power	Digital swelling by Jeweller's ring, ESR, WBC, Hb, hematocrite	Morning stiffness, pain, fatigue, tenderness	Joint findings (heat, effusion, swelling), range of motion
Lowman (1958)	ADL (106 activities of daily living)			
Wallace & Ragan (1958)		ESR, Hb	Morning stiffness, aspirin need	Fatigue, weakness, joint findings (heat, redness, swelling)
Vaughn, Howell & Keim (1959)	Grip power, walking time		Morning stiffness, joint pain, fatigue, tenderness	Joint findings (heat, effusion, circumference), range of motion
Smyth (1960)	Grip power, walking time	ESR, WBC, hemato-crite, Waaler-Rose test, radiological assessment	Pain, tenderness	Joint findings (heat, redness, effusion), range of motion
Decker *et al.* (1960)			Pain, sleep pattern, ability to limber with activity	Synovitis, secondary fibrositis
Black *et al.* (1960)		Digital swelling by Jeweller's ring ESR ,CRP	Pain on motion, tenderness, morning stiffness	Joint swelling, range of motion, functional capacity
Scott (1960)		Stiffness mp-joint II by extension spring		

Author	1 Patient's capacity	2 Objective findings	3 Patient's interpretation	4 Examiner's interpretation
Wright & Johns (1960)		Stiffness mp-joint II by strain gauges		
Hollander & Young (1963)			Tenderness by palpameter	
Smyth, Velayos & Hlad (1963)		Hand- and foot volume by water displacement		
Boas (1964)		Joint heat by infrared camera		
McCarty (1965)			Tenderness by dolorimeter	
Buchman (1965)	Functional tests	ESR, Hb		Joint involvement, systemic disturbance
Brånemark *et al.* (1965)		Joint heat by infrared camera		
Cosh & Ring (1967)		Joint heat by infrared camera		
Rice (1967)		Stiffness mp-joint III by pendulum damping		
Ingpen & Kendall (1968)		Stiffness mp-joints by timing a 10-degree free fall		
Haberman *et al.* (1968)		Joint heat by infrared camera		

Some of the methods listed in Table 1 (e.g., Empire Rheumatism Council, 1955, Shetlar et al., 1956) have been used to correlate systemic disease activity with serum values of acute phase reactants, e.g., serum mucoid levels (Feldman & Markham, 1961), C-reactive protein levels (Nettelbladt & Sundblad, 1962), erythrocyte sedimentation rate (Böttiger, Malmquist & Olhagen, 1964). The method of Wallace & Ragan (1958) was used to correlate clinical disease activity with serum levels of rheumatoid factor (Sievers, 1965). Engstedt & Strandberg (1966) used the method of Shetlar et al. (1956) in a comparison between clinical activity and hematological data in RA.

As can be seen in Table 1, numerous criteria are based on the patient's or on the examiner's subjective opinion concerning the condition while proportionately little attention is paid to the patient's functional capacity. It has perhaps been feared that patients would not in general participate in functional tests with sufficient motivation due to psychological factors.

In discussing drug evaluation in RA, Smyth (1960) says: "Anyone who has made a serious attempt to grade results of therapy in rheumatoid arthritis recognizes that there are symptomatic responses that are so elusive and personal that they cannot be evaluated on a statistical basis. Unfortunately, these are the very factors about which the patients are most concerned—stiffness, muscle spasm, weakness, anorexia, fatigue and lack of sense of well-being."

Fosdick (1968) defines a complete remission in RA: "Subjective: A generalized feeling of well-being without fatigue, absence of pain, stiffness or weakness beyond that of poor mechanical function. Residual symptoms consist of irreversible mechanical problems from previously existing joint damage. Objective: Improvement in muscle strength and absence of heat, swelling, redness and tenderness of joints. Laboratory: Normal erythrocyte sedimentation rate."

Among objective findings in Table 1, methods for joint temperature estimation and joint stiffness registration have been listed and during recent years more attention has been paid to the use of them. Among functional tests in column 1, gripping strength determinations have maintained their popularity especially in drug tests, this being, however, the only test of muscle weakness that has been in common use.

The present investigation was planned in order to obtain additional information about the value of a systematic evaluation of joint temperature, joint stiffness and muscle strength in rheumatoid arthritic patients treated under routine conditions. Three methods were investigated:

1. Infrared thermography for heat emission measurement of joints.
2. Visco-elastic joint stiffness registration in metacarpo-phalangeal joints.
3. Determination of maximal voluntary isometric muscle strength.

In the following investigation these methods will be presented and their application in different evaluating problems concerning patients with RA will be discussed.

Chapter 1

INFRARED THERMOGRAPHY IN RHEUMATOID ARTHRITIS

Heat, being one of the four classical signs of inflammatory activity, is generally accepted as an indication of altered local circulatory conditions and tissue metabolism, changes significant of inflammation. Direct measurement of intra-articular and periarticular temperatures have been made in patients with RA in assessing joint inflammation (Horvath & Hollander, 1949, Brånemark, Laine, Lindström & Vainio, 1963). These authors used a thermocouple introduced directly into the synovial cavity and they also measured the skin temperature over the joint.

Since Lawson put the detection of infrared radiation to medical use in 1956, Lloyd Williams et al. (1960), Boas (1964), Brånemark et al. (1965, 1967), Cosh (1966), Cosh & Ring (1967), Haberman et al. (1968) and Goldie (1969) have applied this principle as an adjuvant in the assessment of rheumatic disease. The methods and their application in different fields of medicine have been discussed at a conference held in New York City in 1963.[1] A survey on the current status of medical thermography was given by Gershon-Cohen, Haberman-Brueschke & Brueschke (1965). At a meeting in Strasbourg, Brånemark (1967) gave an account of the infrared thermography (IRT) technique used in this investigation (AGA Thermovision). A report on the IRT technique in the evaluation of RA using the same equipment was given at the XII Nordic Congress of Rheumatology in Helsingfors in 1968 (Tiselius).

It is the aim of this study to further investigate what information the IRT technique can provide in routine rheumatological diagnostic and evaluative work. A description of the IRT method using the AGA equipment and comments on alterations in the thermograms following different forms of anti-rheumatic therapy will be given. The relation between emission pattern over joints and clinical as well as laboratory data concerning the arthritic patient will be reported on in a different section of the present investigation.

METHODS

Theoretical Background

Infrared waves radiate from a surface in accordance with known physical laws and in proportion to the absolute temperature of that surface. All bodies

[1] Published in a Monograph of the New York Academy of Sciences, vol. 121, 1964.

Fig. 1. The AGA Thermovision equipment. Camera unit to the left and display unit to the right.

with a temperature exceeding absolute zero emit electromagnetic radiation and the spectral character and intensity of the infrared waves are determined by the absolute temperature.

The total radiation emitted by an object is proportional to the product of its area, the fourth power of its absolute temperature, its emissivity and a constant, the Stefan-Boltzmann constant. This law can be written as

$W = \varepsilon \sigma T^4$ (the Stefan-Boltzmann law, derived from Plank's equation)

where W is the radiant energy per unit area, ε is the emissivity, σ is the Stefan-Boltzmann constant and T is the absolute temperature in degrees Kelvin. The emissivity for a black body which absorbs all and reflects none of the radiation falling upon it is $\varepsilon = 1.00$. Hardy (1934) has pointed out that human skin is as near a black body as can be detected by experiment, $\varepsilon = 0.986 \pm 0.1$ and that the presence of water vapour and CO_2 in the layers of air next to the skin does not appreciably affect the radiation from the surface. Mitchell, Wyndham & Hodgson (1967) confirmed the work of Hardy, and Watmough & Oliver (1968) concluded that the emissivity in vivo of human skin at normal incidence lies in the range $1 > \varepsilon \geqslant 0.98$. Human skin emission reaches its maximum energy level at about 10 microns with a range between 2 and 20 microns. It is an almost perfect emitter of infrared radiation in the spectral range within these limits (Barnes, 1963). As regards the emissivity of the human skin there is a lack of

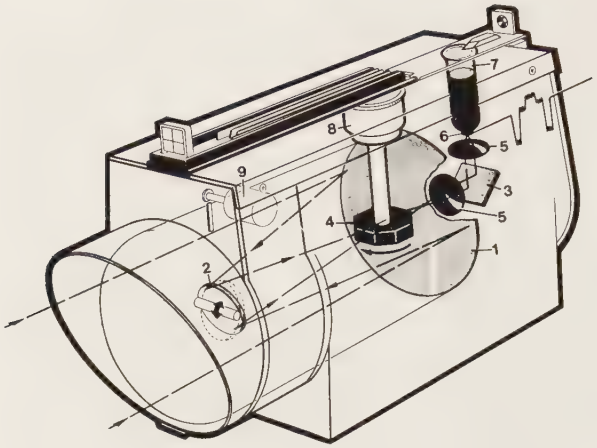


Fig. 2. Schematic drawing of camera unit. 1. Spherical mirror. 2. Tilting mirror, oscillating at 16 cps. 3. Plane mirror. 4. Silicon prism rotating at 200 rps. 5. Germanium lens. 6. InSb detector. After preamplification the video signal is fed to the display unit. 7. Dewar flask for liquid nitrogen. 8. Motor for prism. 9. Motor for tilting mirror.

knowledge about the influence caused by pathological conditions involving the skin itself. If considerable changes in emissivity do occur, temperature determinations using IRT might give inaccurate information about the inflammatory condition.

Infrared radiation can be illustrated with the aid of a detector sensitive in this part of the spectrum. Such detectors are made of, for instance, indium antimonide or germanium and require cooling for optimum sensitivity with liquid nitrogen or liquid helium.

Equipment

In the present investigation AGA Thermovision equipment has been used. It consists of a camera with an infrared television system that presents the temperature distribution of an object as an image on a cathode ray tube (Fig. 1). The AGA system was chosen because of its built-in isotherm function.

Camera Unit

An optical system scans the field of view at a very high speed and focuses the infrared radiation on an indium antimonide detector cooled with liquid nitrogen. The detector converts the radiation signal into an electrical signal which is fed into the display unit. An image of the field of view is formed by a primary spherical mirror and a secondary plane mirror. The latter tilts round a horizontal axis at 16 cycles per second producing 16 frames per second. A square silicon prism rotating at a speed of 400 revolutions per second transfers the image to the plane of a small aperture. Four lines are scanned each revolution resulting in 1600 lines per second. After passing through a preamplifier in the

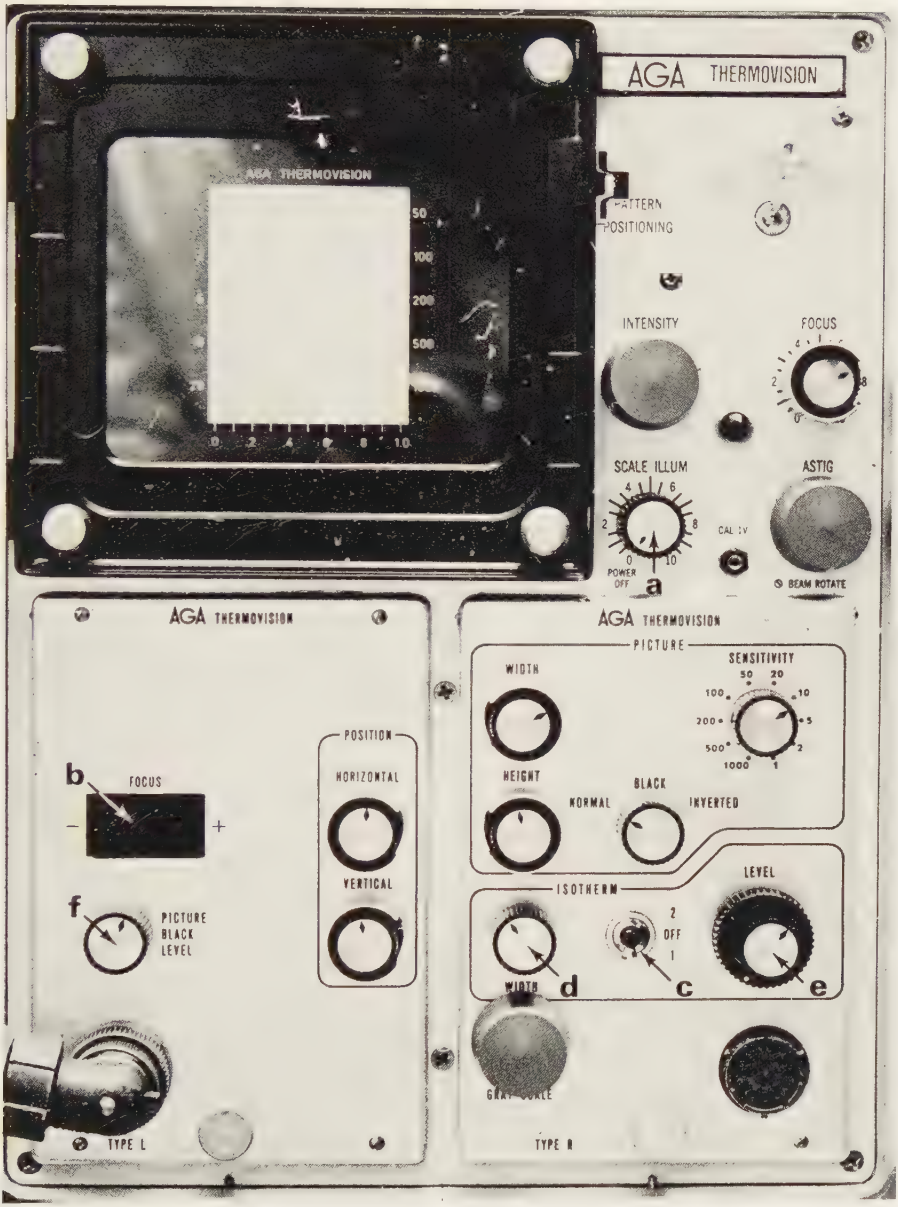


Fig. 3. Front of oscilloscope illustrating the different controls and the steps in the calibration procedure. (*a*) Starting the camera; (*b*) focusing the reference spot; (*c*) initiating the isotherm function; (*d*) adjusting the isotherm width to cover 2.0 C; (*e*) adjusting the isotherm marker to scale point 0.5 in its middle; (*f*) adjusting the picture black level until the complete white reference spot is just disintegrated. For further explanation, see text.

Fig. 4. Right knee of a patient with RA illustrating the heat emission pattern before (*left*) and after (*right*) plotting the isotherm in the picture. The patella region is cooler (*darker*) than the surrounding warmer (*lighter*) parts of the knee joint. The distribution of inflamed tissue with a temperature of this specific level is clearly illustrated with the aid of the isotherm spot in complete white.

camera, the detector signal is fed into the display unit. The wavelength band utilized is 2.0 to 5.4 microns. In Fig. 2 a schematic drawing of the camera unit is given.

Display Unit

This is an oscilloscope with a 5-inch screen and fitted with special plug-in units. The signal from the camera is amplified and processed before being used to modulate the intensity of the beam in the picture tube. The beam sweeps across the tube face in a pattern corresponding to the scanning pattern of the camera. Camera focusing can be adjusted from the display unit and corret focusing is checked by observing the picture on the screen. Fig. 3 shows the front of the oscilloscope with its different controls.

Isotherm Function

By plotting isotherms directly in the picture on the screen temperature evaluation can be effected in a convenient manner. All areas with equal temperatures are marked in complete white. Any temperature can be selected along a temperature scale by turning a dial. Areas at a particular temperature are then shown

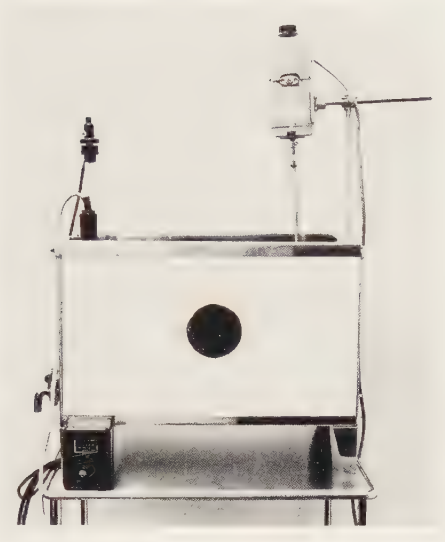


Fig. 5. Water bath with infrared radiation reference source appearing as a black spot. The water temperature is kept at a constant level with the aid of a thermostatic heating device.

up in the picture by increasing their light intensity to complete white. The width of the isotherm can be varied. In Fig. 4 an inflamed knee joint before and after plotting the isotherm in the picture is illustrated.

To produce permanent records of the picture a Hasselblad camera, model 500 EL, has been used. It is attached to the oscilloscope screen. Kodak Verichrome Pan film was used. Exposure time: 0.5 second.

For further information concerning the camera, see Björk (1966).

Infrared Radiation Reference Source

As I have earlier pointed out (Tiselius, 1968) the need for an infrared radiation reference source with a constant temperature and emissivity for calibration of the infrared camera is of great importance if serial thermograms are used in judging alterations in local joint heat from one time to another in the same patient. For this purpose a water bath was used holding a constant water temperature of 28.2°C. The temperature was kept constant with the aid of a thermostat-controlled heating device. The temperature level was found suitable for calibration purposes in studying heat emission from joints empirically. The glass wall in front of the water bath was painted black in order to minimize reflection. A screen made of stiff paper with a circular opening measuring about 10 cm in diameter was placed in front of the black painted glass wall. The black circular spot thus appearing served as an infrared radiation reference source with a constant temperature level throughout the investigation. The radiation source is illustrated in Fig. 5.

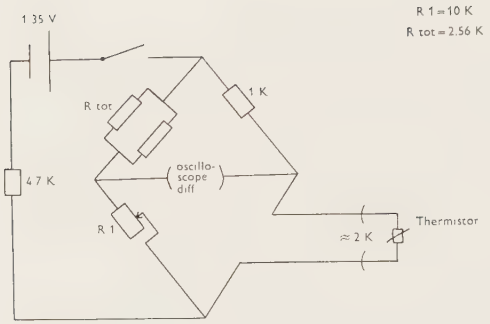
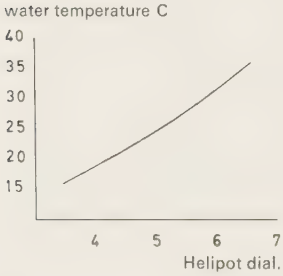


Fig. 6. Thermistor with bridge for control of reference temperature.

The temperature constancy of the reference source was checked in the following way:

A very small thermistor with a diameter of 0.355 mm (type GC 32 J 3 Fenwal Electronics) was connected to a bridge as indicated in Fig. 6. The thermistor was selected so as to make it possible to register rapid fluctuations in the reference temperature and to minimize the temperature gradient due to its own warming up. The thermistor bridge was calibrated against known water temperatures measured with a mercury thermometer. The bridge was balanced for each temperature using a potentiometer. As a base indicator a cathode ray oscilloscope with a differential input and a sensitivity range of 5 mV was used. A calibration curve with water temperature on the vertical axis and the potentiometer dial on the horizontal axis was drawn (Fig. 7) showing good linearity. The thermistor was then attached to the reference source and a check on its temperature constancy was performed in a room with a known stable temperature regulated by a thermostat. A slight variation within 0.3°C in the reference temperature was found. This was probably caused by the entrance of two people into the room or by a routine thermographic examination where three persons took part. This illustrates how sensitive the reference source is to external heat radiation and how important it is to strive for a constant room temperature avoiding circulation of persons and draught in the examination room during scanning. Results of the constancy control are given in Table 2.



Temp. C°	Dial. Helipot	Temp. C°	Dial. Helipot
36.0	6.58	25.0	5.15
32.0	6.13	24.5	5.06
30.5	5.95	22.5	4.70
29.0	5.70	19.5	4.20
27.5	5.50	16.0	3.46

Fig. 7. Calibration curve obtained with the thermistor bridge when calibrated against known water temperatures.

Table 2. *Variations in the reference temperature illustrating how sensitive the reference source is to external heat radiation.*

Water temperature was constant during the test. For explanation, see text.

	Time	Helipot dial	Reference temperature	Water temperature
Two persons in the room	19.12	5.59	28.2	28.2
	19.20	5.61	28.3	28.2
	19.25	5.61	28.3	28.2
	19.35	5.61	28.3	28.2
One person in the room	08.15	5.63	28.4	28.2
	08.55	5.66	28.6	28.2
	09.15	5.64	28.5	28.2
	09.45	5.64	28.5	28.2
Thermography three persons entered the room	10.15	5.64	28.5	28.2
	10.35	5.63	28.4	28.2
	11.45	5.62	28.3	28.2
	13.30	5.62	28.3	28.2
	14.40	5.62	28.3	28.2

Calibration Procedure

In order to balance the infrared camera system against the reference source from time to time before thermal scanning with a view to making comparative studies of thermograms more reliable, a calibration procedure has to be followed before every examination as indicated below (Fig. 3).

The camera is allowed to run for at least ten minutes and liquid nitrogen is supplied. It is then directed towards the radiation reference source which is situated at a distance of five meters. The black circular spot shows up as a bright circle on the oscilloscope screen and the camera is focused on the circle which is as centrally located as possible. The isotherm function is then initiated and the width of the isotherm marker on the grey scale at the bottom of the picture is adjusted to cover 2.0 C. This is the distance between two adjacent scale points using a temperature range of 20°C indicated on the left side of the picture. The width of the isotherm and the temperature range can be varied, but the above mentioned values have beeen found suitable for routine work empirically and have been used throughout the investigation. The grey scale at the bottom of the picture thus represents a temperature range of 20°C and it has been suitable for clinical work to let scale point 0.5 represent the calibration point to which the isotherm marker is adjusted with the scale point in its middle. The level of blackness in the picture is then adjusted until the complete white reference circle on the screen is just being disintegrated (Fig. 8). This position is very sharply marked and any deviation of the isotherm marker results in either a complete black or a complete white reference spot. Using the

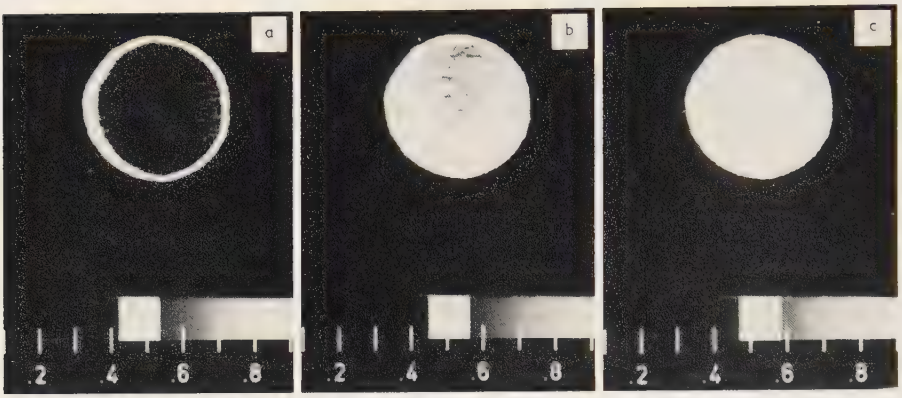


Fig. 8. Reference spot during calibration. At scale point 0.5 it is just being disintegrated (*b*). Any deviation of the isotherm marker (*a* and *c*) results in a complete black or a complete white spot. The calibration point can thus be very sharply marked.

reference source in this manner ensures that the infrared camera system is balanced in an appropriate manner to permit comparative thermography before each examination. The calibration then has to be checked every now and then for temperature drift, at least during prolonged use of the camera. There will always be some variation. However, if these precautions are taken, the examiner may be certain that the infrared camera is producing pictures of the clinical conditions on different occasions in an identical way, provided that the patient is placed at the same distance before each examination. Any variations in the pictures can thus be related to changes in pathology or activity of the diseased condition by means of different heat emission patterns.

Clinical Application

All examinations with the infrared camera in the present investigation were made in a room kept at a controlled temperature of 18–20°C. The bare extremities of the patient were cooled at room temperature for 15 minutes, during which time the camera was allowed to run. The patients were asked not to smoke (see Ryan, 1969) or eat heavy meals before the examination. Heavy meals might alter peripheral circulatory conditions. The calibration procedure was undertaken before each examination. The patient was placed in a standing or sitting position in front of the camera at a distance of five meters. This distance was kept constant throughout the investigation. The infrared radiation reference source was situated on the left side of the patient at a distance of about two meters. Fig. 9 illustrates the relation between the camera, the patient and the reference source. After the calibration procedure the camera was turned towards the patient and the joint in question was adjusted to the center of the

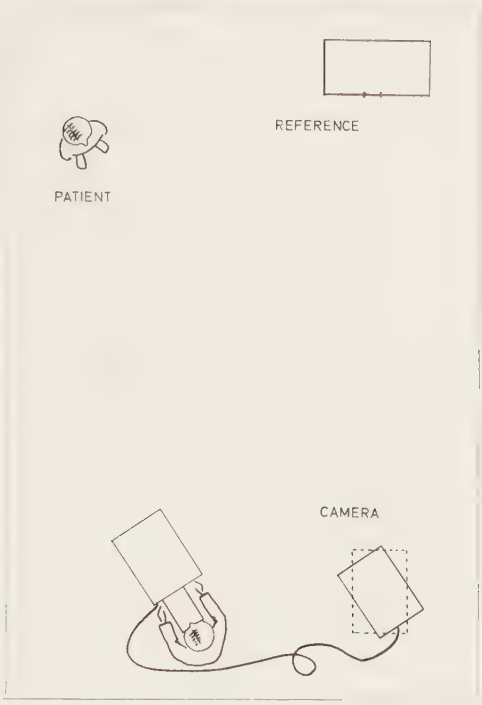


Fig. 9. Position of the infrared camera, the patient and the reference source during scanning. The patient is placed at a distance of five meters from the camera with the reference source two meters to the left.

picture and focused. The isotherm function was then initiated and the marker on the grey scale at 0.5 was turned to the right in order to illustrate the warm parts of the joint in complete white. This usually occurs with the isotherm marker situated between 0.6 and 0.9 since the skin temperature of active joints often reaches this level. This does not mean that the skin temperature is determined in absolute degrees with this method, the point of interest being differences in temperature rather than true temperature values. Before exposure, the isotherm level which gives an instructive and informative picture of the warm, inflamed joint is selected and noted *because on all following examinations of that joint exactly the same isotherm level has to be used if quantitation of serial thermograms is intended.*

Projections of Joints

The projections of joints commonly used during scanning are illustrated in Fig. 10. It is important that the joint being studied is adjusted to the exact center of the picture. Any deviaton will cause alterations in the thermograms, which may give false information about the temperature distribution. This phenomenon will be further discussed below.

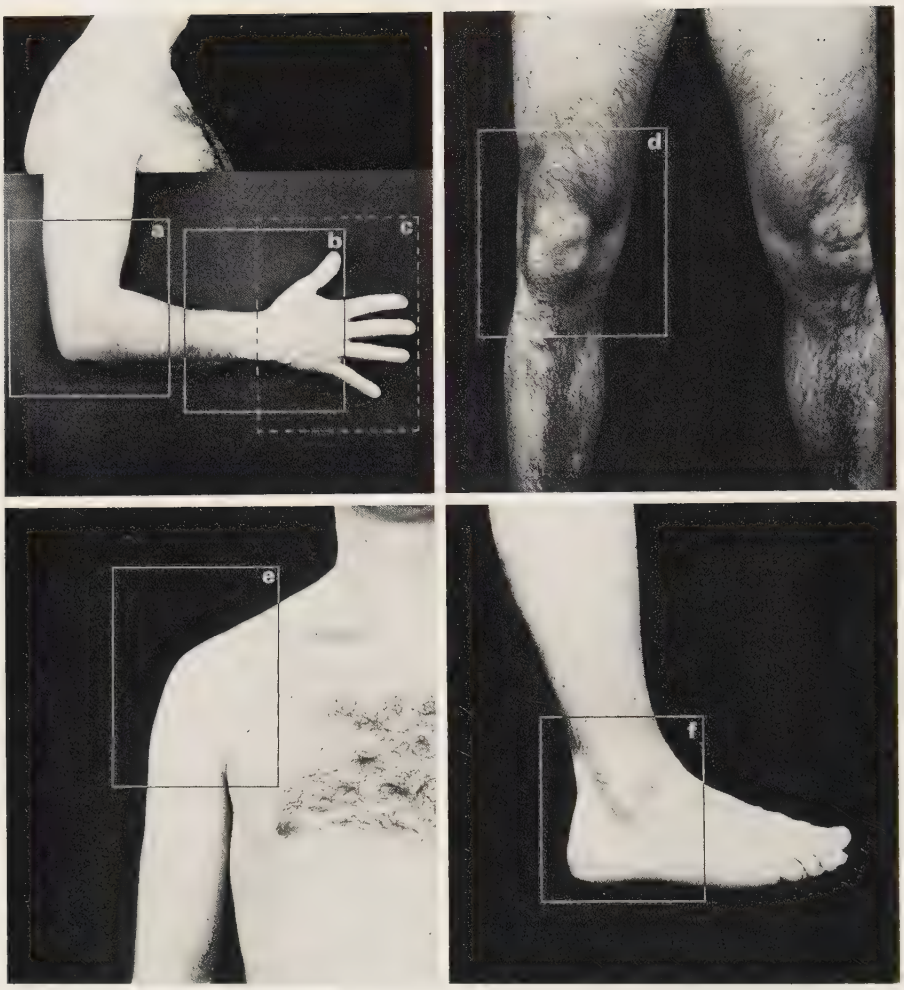
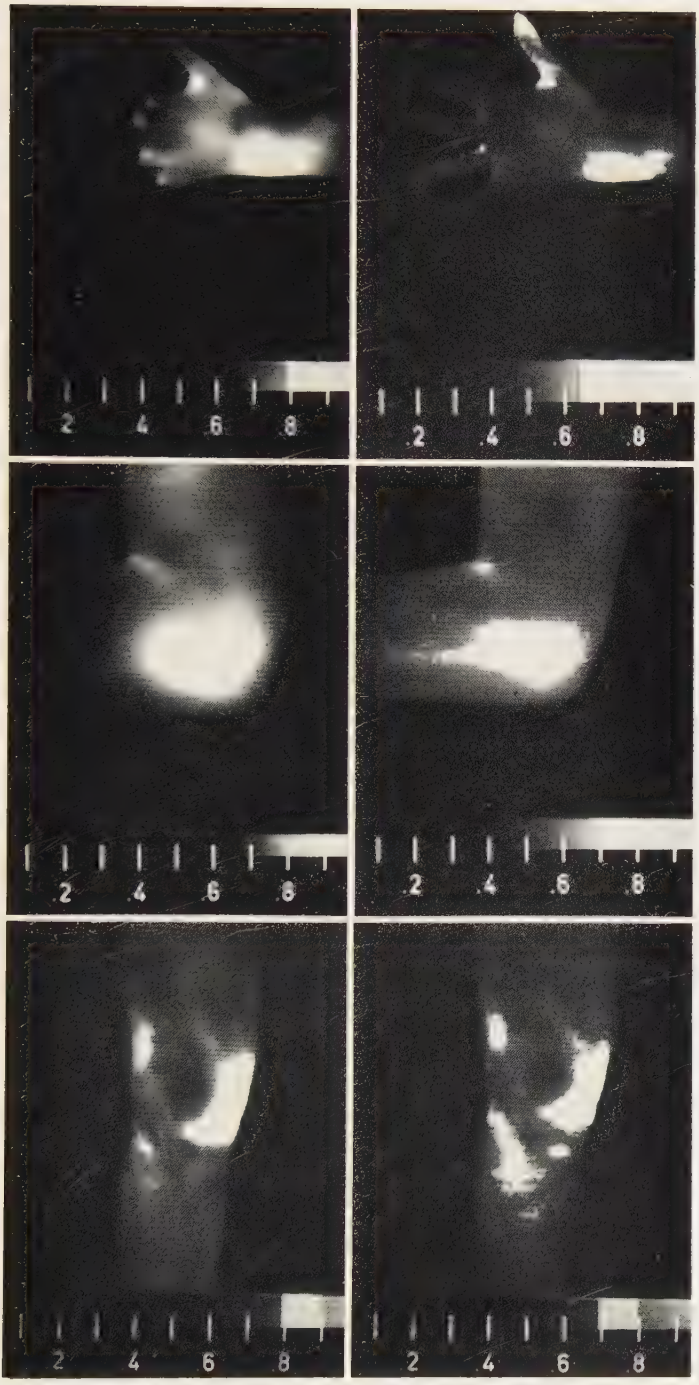


Fig. 10. Joint projections commonly used. The joint should be adjusted to the center of the picture. (*a*) Elbow; (*b*) wrist; (*c*) hand; (*d*) knee; (*e*) shoulder; (*f*) ankle.

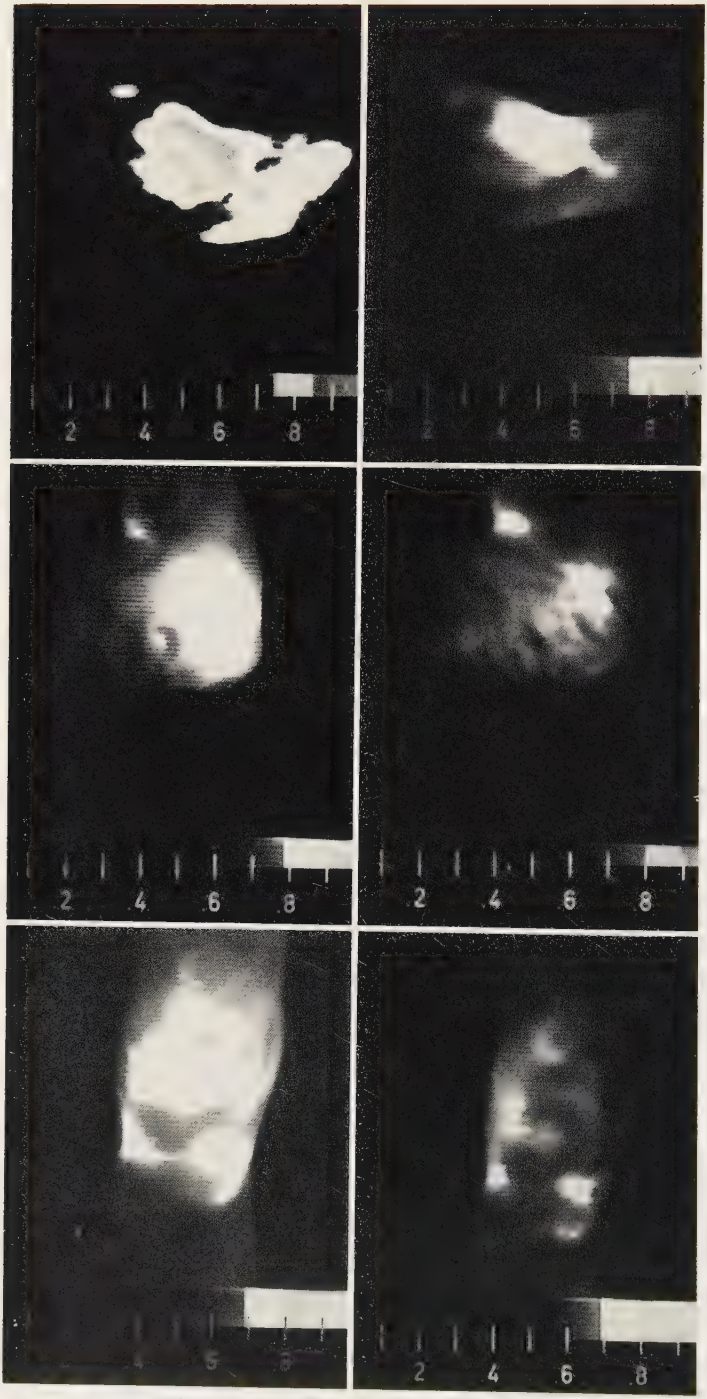
Quantitative Methods in the Assessment of Thermograms

Brueschke, Haberman & Gershon-Cohen (1964) have pointed out that probably the greatest error in the quantitative analysis of an infrared thermogram is due to the human factor. This is because comparison of the density

Fig. 11. Method I. The isotherm level is varied and the isotherm surface is kept as constant as possible. The caput ulnae region shows a temperature decrease of 3.0 C between occasions *A* and *B*. In the same way the temperature decrease of the elbow can be calculated to be 3.0°C and of the knee to be 2.0 C. Temperature difference between two adjacent scale points is 2.0 C using a sensitivity of 20 indicated on the oscilloscope front.



A B



A B

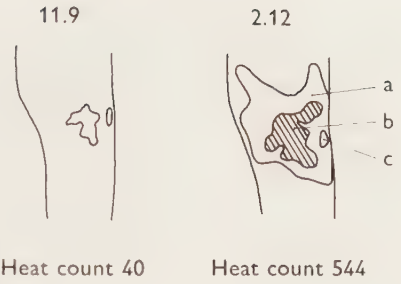


Fig. 13. Isotherm spot on two different occasions from a rheumatoid knee joint. The spot is plotted on paper and its surface is measured with a planimeter. The lined area on the right spot (2.12) indicates higher and the small area lateral to it indicates lower temperature levels than the isotherm width of 2.0°C. The heat count of the right thermogram (2.12) is calculated by adding surface *b* to and subtracting surface *c* from the original surface, i.e., heat count $= a + b - c$ (arbitrary units).

of areas on the patient's thermogram with a known calibration grey scale is difficult and is subject to considerable individual interpretation. They therefore designed an electronic relative densitometer which permits determinations of light transmission with a photocell through various parts of the film with a high degree of accuracy.

The following two methods are suggested for quantitation of thermograms of inflamed joints. It is assumed that the above mentioned calibration procedure has been carefully followed.

Method I

Fig. 11 illustrates the use of this method. On occasion *A* the isotherm level which gives an instructive picture in complete white is selected. On occasion *B* roughly the same picture appears at a lower isotherm level. The distance between isotherm marker on occasions *A* and *B* indicates the temperature difference. This method can be modified to measure the difference between temperature maxima on both occasions by adjusting the isotherm level a little more to the right towards higher temperatures thus using the scale point where complete white just disappears from the picture. This method, in which the isotherm level is varied using identical pictures or hot spots of the joint, has a limited value from a clinical point of view. It demonstrates temperature differences between only the warmest parts of the diseased condition on different occasions, but it does not tell about alterations in the distribution of inflamed tissues at a certain temperature elevation. On the other hand it allows comparisons beyond 2.0°C in temperature differences.

Method II

This method utilizes the surface of the spot pictured in complete white with the aid of the isotherm function. The same isotherm level is used on each occasion

Fig. 12. Method II. The isotherm level is kept constant and the isotherm surface is measured on occasions *A* and *B*. In this way heat counts are obtained and used in the quantitation of thermograms.

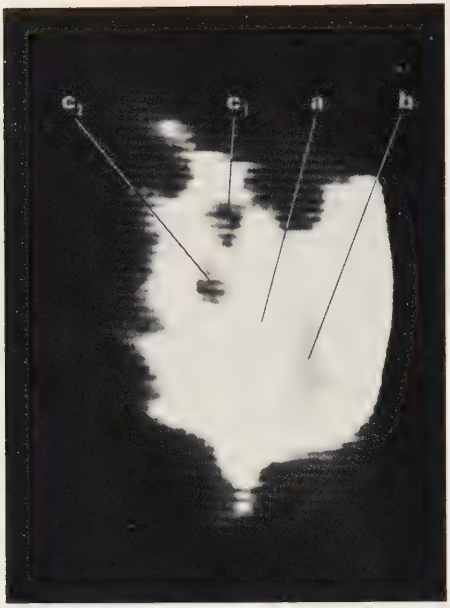


Fig. 14. Left knee of a patient with RA. Heat count $= a + b - (c_1 + c_2)$.

in studying variations in the complete white area. From a clinical point of view this method is more instructive and gives more details about the distribution and activity of the inflammatory process. Fig. 12 illustrates the principle of method II. The thermal picture on the film is enlarged to the same degree each time and the border of the hot spot in complete white is plotted on a paper (Fig. 13). The surface is then determined using a planimeter which gives a numerical value, the *heat count*, in arbitrary units of the area of interest. Sometimes, however, it happens that temperature variations within the spot are greater than 2.0°C. Warmer and cooler areas will then appear darker beyond the limits of the isotherm marker and it must be noted during the examination if dark areas appear in the complete white image and if these areas represent warmer or cooler spots. This cannot be judged directly from the film. Only by moving the isotherm level in both directions during the examination can these dark spots be interpreted. A picture such as that in Fig. 14 may thus be analyzed and quantitatied by adding warmer areas to and subtracting cooler ares from the originally determined surface. This seems to be a reasonably accurate way of solving the quantitative problem from a clinical point of view. A heat count in arbitrary units thus gives information about the inflammatory process. Changes in heat counts can then be expressed either in arbitrary units or in percentage of the original surface.

It sometimes happens that the inflammatory process has altered its intensity more than 2.0°C in either direction, thus making method II, in which the iso-

Table 3. *Clinical and laboratory data on 71 cases of RA.*

Classification . . .	"Classical" RA	"Definite" RA	"Classical" RA/ "Definite" RA
Number of cases	41	30	
Females	26	19	
Males	15	11	
Average age (years)			
Females			50.6
Males			56.0
Average duration of arthritis (years)			
Females	15.7	7.4	
Males	9.6	5.1	
Stage			
I	4	22	
II	25	7	
III	12	1	
IV	0	0	
Pos SSCA	40	19	

therm level is constant and the thermal picture varies, less useful. The complete white spot has then disappeared from the picture and the heat count equals zero. If this happens one gets at least the information that the intensity has decreased or increased more than 2.0 C. The isotherm function is then used in order to analyze the thermal pattern which will then appear at lower or higher temperature levels and, if possible, make identical pictures visible in order to assess them according to method I.

CLINICAL MATERIAL

Mode of Selection

The thermographic examinations were performed on patients admitted to the Department of Rheumatology, Regionsjukhuset, Örebro from October 1967 until December 1968. There were 54 inpatients and 17 outpatients selected from cases of "classical" or "definite" RA. All patients were selected according to different forms of treatment. The RA cases were denoted as "classical" if 7 or more of the American Rheumatism Association criteria (1958) were present. "Definte" cases required 5 of the criteria.

Subjects

"Classical" RA: 41 patients, 26 females and 15 males. Rheumatoid progression according to Steinbrocker, Traeger & Batterman (1949): 4 patients were in stage I, 25 in stage II, 12 in stage III and none in stage IV.

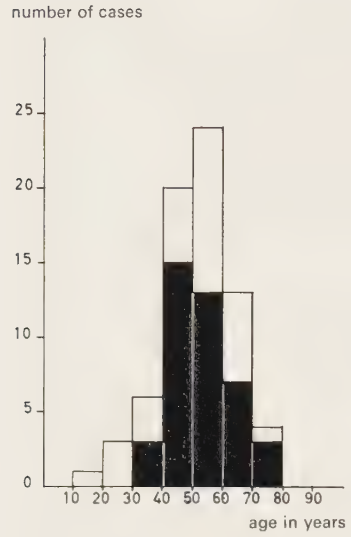


Fig. 15. Age distribution in 71 cases of RA. ■ = "classical" RA; □ = "definite" RA.

"Definite" RA: 30 patients, 19 females and 11 males. 22 patients were in stage I, 7 in stage II, 1 in stage III and none in stage IV.

The mean age in the female group was 50.6 years, in the male group 56.0 years. The duration of the disease defined as the period of continuous joint symptoms ranged from 1 to 32 years, two patients in stage II however maintained that they had suffered from joint symptoms for as long time as 35 and 54

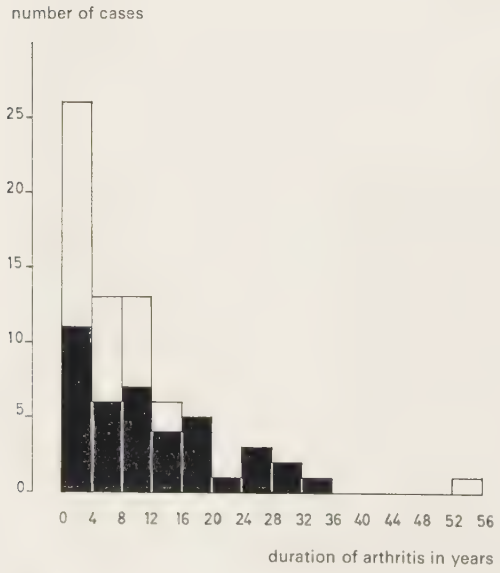


Fig. 16. Duration of continuous joint symptoms in 71 cases of RA; ■ = "classical" RA. □ = "definite" RA.

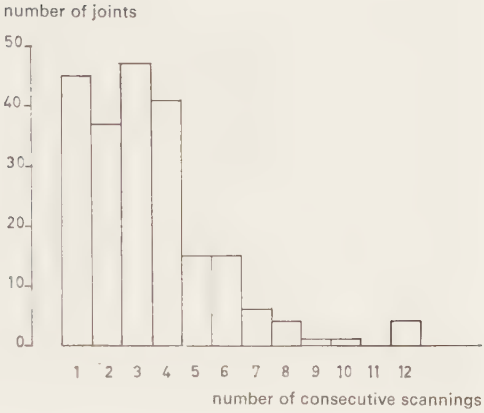


Fig. 17. Number of joints distributed over number of scannings. Usually between one and six scannings of the same joint have been performed. The hand is counted as one joint for simplification.

years, respectively. The average duration was 15.7 years for "classical" females, 7.4 years for "definite" females, 9.6 years for "classical" males and 5.1 years for "definite" males. The two cases with durations of 35 and 54 years were not counted because of the uncertainty in their statements. Table 3 shows some clinical and laboratory data of the seventy-one patients with RA. In Fig. 15 the age distribution can be seen and Fig. 16 illustrates the duration of joint disease.

Treatment

In addition to conventional therapy including intraarticular administration of hydrocortisone, different forms of local treatment were applied. Twelve

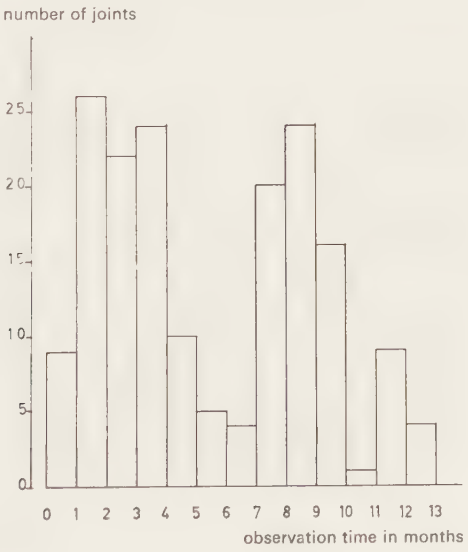


Fig. 18. Number of joints observed during different periods of time. The hand is counted as one joint for simplification.

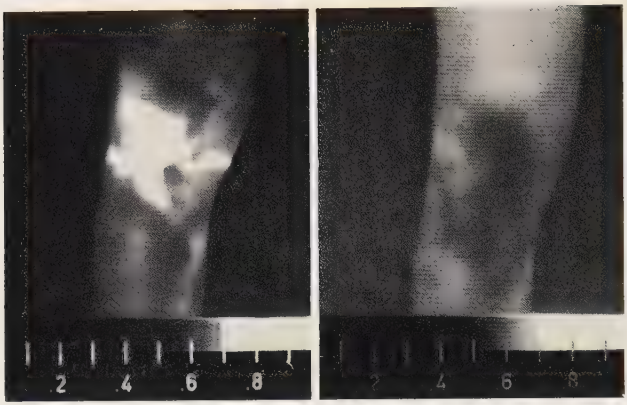


Fig. 19. Heat emission from a rheumatoid knee before (*left*) and after one week of bed rest (*right*).

patients received intraarticular treatment with colloidal radioactive gold,[1] eight in one knee, three in both knees and one in the left shoulder. Twenty-five patients underwent synovectomy,[2] sixteen in one knee, eight in both knees and one in the left ankle (tendon sheath). In five patients popliteal cysts were removed.[2] In a few cases with early and very active signs of local joint inflammation the effect of various antirheumatic agents such as ACTH, Prednisolone, Phenylbutazone and Oxyphenylbutazone has been evaluated. During the evaluation period no other form of treatment besides the basic program was started.

Methods of clinical and laboratory examination

Each patient was examined by the author on admission to hospital. Besides the general physical examination the articular manifestations were evaluated with regard to limitation of motion, pain at rest and at motion, type and degree

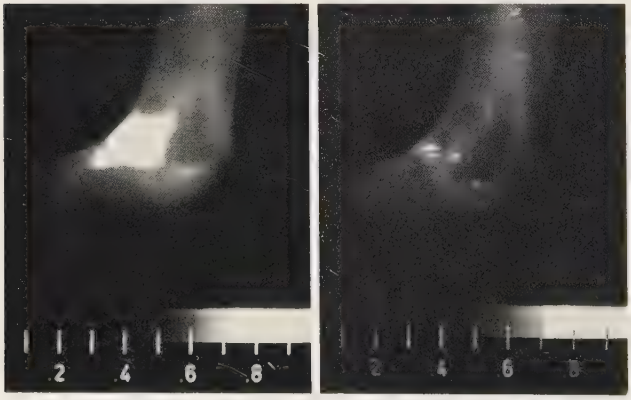


Fig. 20. Left ankle of a patient with RA before (*left*) and after one week in bed (*right*).

[1] Department of Radiotherapy, Regionsjukhuset, Örebro, Sweden.
[2] Department of Orthopedic Surgery, Regionsjukhuset, Örebro, Sweden.

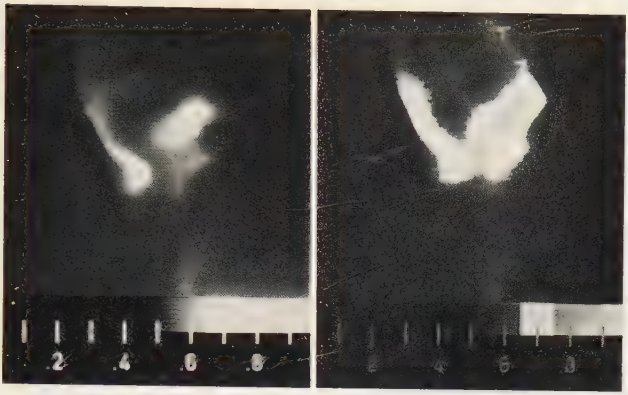


Fig. 21. Left knee of a patient with RA before (*left*) and after one week of daily vigorous contractions of the quadriceps. A marked increase in heat emssion from the joint is noted.

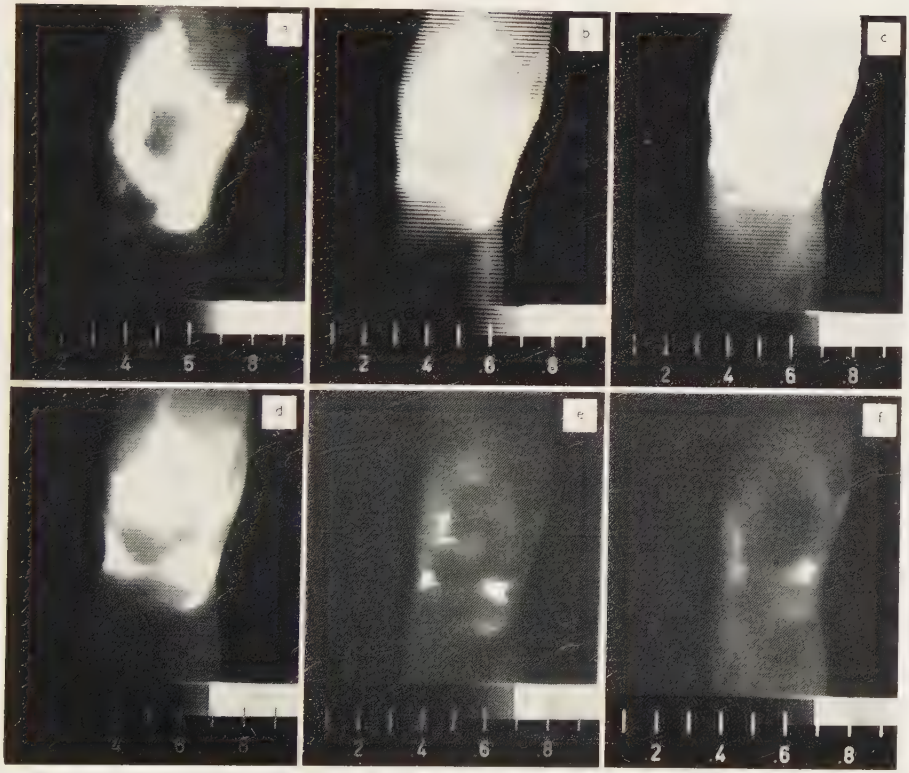


Fig. 22. Synovectomy of right knee of a patient with RA. (*a*) Emission pattern on admission to the department; (*b*) appearance after one week of physical therapy and quadriceps exercises; (*c*) marked increase in heat emission six days after surgical synovectomy; (*d*) one month; (*e*) two months; and (*f*) eight months after surgery.

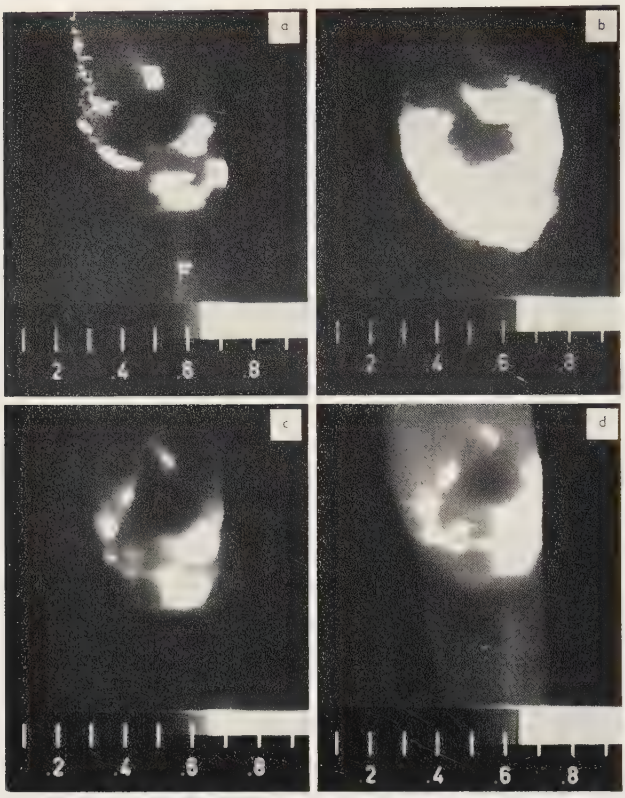


Fig. 23. Synovectomy of left knee of a patient with RA. (*a*) Emission pattern on admission to the department; (*b*) two weeks after surgical synovectomy; (*c*) five months; and (*d*) nine months after surgery. Emission patterns show sustained activity.

of capsular swelling, presence of effusion and deformity. Extraarticular lesions such as tenovaginitis, nodules and cysts were recorded. X-ray examination of affected joints was carried out under routine conditions[1] as were the laboratory tests for rheumatiod factor,[2] paper electrophoresis on serum[3] and erythrocyte sedimentation rate according to Westergren.

The thermographic examinations were all made by the author according to the method outlined above. It usually took place after the patient had been hospitalized for a few days while waiting for the treatment program to be selected and always the day before it was initiated. Thus the clinical material was selected according to different forms of treatment and individual thermographic follow-up programs were outlined accordingly.

The number of thermographic examinations on each individual patient varied from one single scanning of one or several joints to serial scannings of one or

[1] Department of Roentgenology, Regionsjukhuset, Örebro, Sweden.
[2] Department of Bacteriology, Regionsjukhuset, Örebro, Sweden.
[3] Department of Clinical Chemistry, Regionsjukhuset, Örebro, Sweden.

Table 4. *Results of intraarticular treatment with colloidal radioactive gold in 15 joints with persistent effusion in patients with RA.*

In the clinical examination absence of palpable effusion is symbolized by —, in the thermographic assessment absence of elevated joint temperature is symbolized by —. Changes in the sedimentation rate must also be noted in judging the effect of the isotope. The improvement in, e. g., joint number 5 might well be due to a decrease in systemic disease activity rather than to a direct effect upon the local joint disease activity caused by beta radiation.

Joint number	Subject	Age	Sex	Classification acc. to A.R.A. (1958)	Stage acc. to Steinbrocker *et al.* (1949)	SSCA	Disease duration in years	Joint treated	Observation time in months	Clinical examination	Thermographic assessment	ESR (erythrocyte sedimentation rate) during observation time
1	R. A.	57	F	class	III	+	10	r k	12	+	+	60–36
2	I. E.	49	F	class	III	+	20	r k	9	+	+	65–48
3	G. J.	59	F	def	II	+	9	l k	8	+	+	12–21
4	G. S.	48	F	class	II	+	10	r k	10	+	+	54–39
5	G. A.	57	M	def	I	+	1	l k	12	—	—	73–13
6	G. A.							r k	3	—	—	20–13
7	R. B.	58	M	class	II	+	2	r k	11	+	+	100–72
8	R. B.							l k	10	+	+	130–72
9	G. H.	62	M	class	II	+	2	r k	10	+	+	88–42
10	K. K.	71	M	class	II	+	3	l s	6	—	+	80–70
11	E. L.	71	M	class	III	+	29	l k	16	—	—	47–40
12	E. L.	59	M	class	III	+	18	l k	12	—	+	76–67
13	G. P.	68	M	def	II	—	54	r k	13	—	—	50–73
14	G. P.							l k	7	+	+	55–73
15	G. R.	59	M	def	I	+	11	r k	12	+	+	21–11

several joints on twelve consecutive occasions (Fig. 17). Observation time reached a maximum of twelve to thirteen months (Fig. 18). A total number of 1080 scannings on 174 different joints was made.

RESULTS

IRT has served as a complement to the routine clinical examination of arthritic patients undergoing different forms of established treatment. Comments on the thermographic findings are given in connection with the illustration of some instructive cases.

Resting the inflamed joint

In early stages of active RA, bed rest providing local rest for the joints is an important form of therapy widely accepted among rheumatologists. A knee joint from a patient with RA showing active inflammation on admission is illustrated in Fig. 19. After one week in bed as the only form of treatment the knee had cooled off and the thermogram revealed a heat pattern that had been nor-

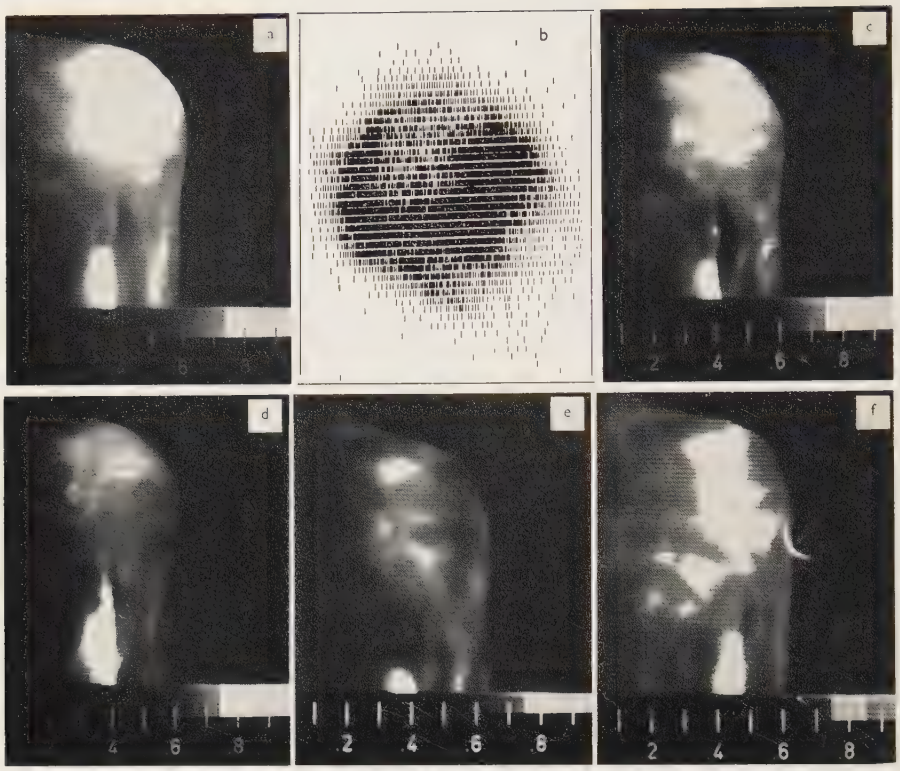


Fig. 24. Left shoulder of a patient with RA treated with radioactive colloidal gold. (*a*) Before injection; (*b*) scintigram showing a satisfactory distribution of the isotope in the joint cavity (lateral aspect) (by courtesy of Dr. Odelberg-Johnsson, Department of Radiotherapy, RSÖ); (*c*) one week; (*d*) two weeks; (*e*) five months; and (*f*) seven months after administration. A relapse has occurred at the time of the last scanning.

malized with the joint region appearing darker than the surrounding area. The same phenomenon in the left ankle of another case of RA is shown in Fig. 20 where one week of bed rest resulted in a marked decrease in heat emission from periarticular tissue.

Physical exercise

On the other hand, vigorous muscle contractions may give rise to increased heat radiation from the adjacent joint indicating a local flare-up. This is illustrated in Fig. 21 where the left knee of a patient with RA is shown before and one week after daily contractions of the quadriceps.

Surgical synovectomy

Regarding surgical synovectomy changes in emission pattern frequently reveal diminished local inflammatory and metabolic activity although in many cases

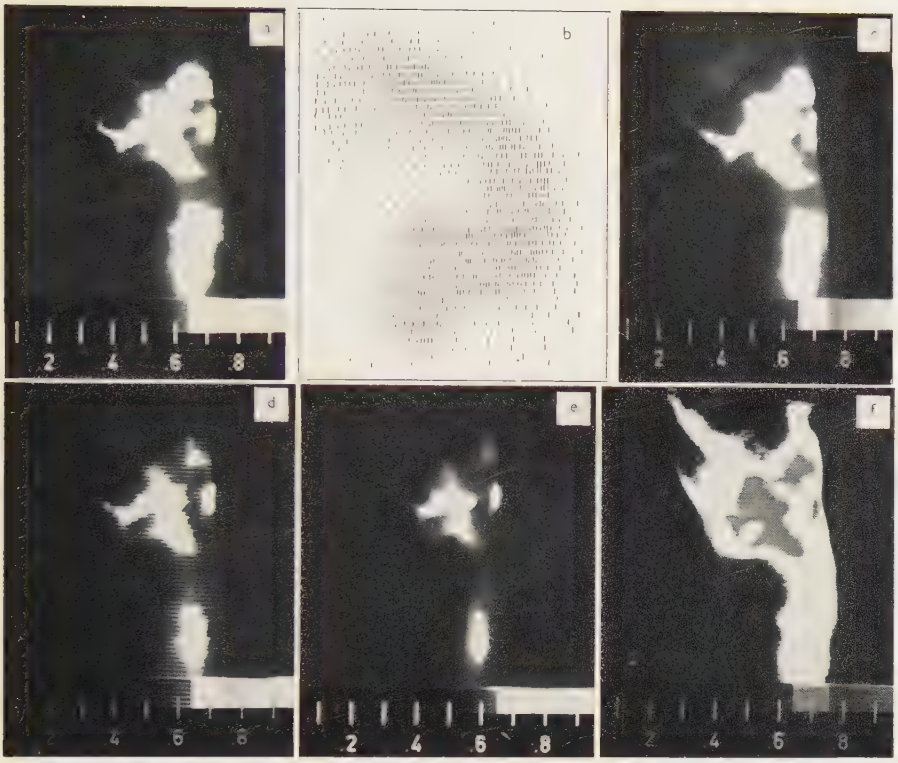


Fig. 25. Left knee of a patient with RA treated with radioactive colloidal gold. (*a*) Before injection; (*b*) scintigram showing a satisfactory distribution of the isotope in the joint cavity (medial aspect) (by courtesy of Dr. Odelberg-Johnsson, Department of Radiotherapy, RSÖ); (*c*) one week; (*d*) two weeks; (*e*) six months; and (*f*) nine months after administration. A marked relapse has also occurred in this joint at the time of the last scanning.

a complete disappearence of white isotherm spots indicating a temperature fall of 2.0°C or more usually does not occur until at least six months following surgery. Fig. 22 shows the result of synovectomy of the right knee joint in a patient with RA observed during a period of nine months after surgery. A marked decrease in local heat emission is noted as early as two months after surgery while in Fig. 23 sustained activity nine months after knee joint synovectomy is obvious. During this time no major changes in the patient's systemic disease activity was noted.

Intraarticular radioactive gold

The use of IRT in evaluating joints following the administration of colloidal radioactive gold seems to indicate that this form of therapy does not result in long standing local remissions as compared to surgical synovectomy of inflamed

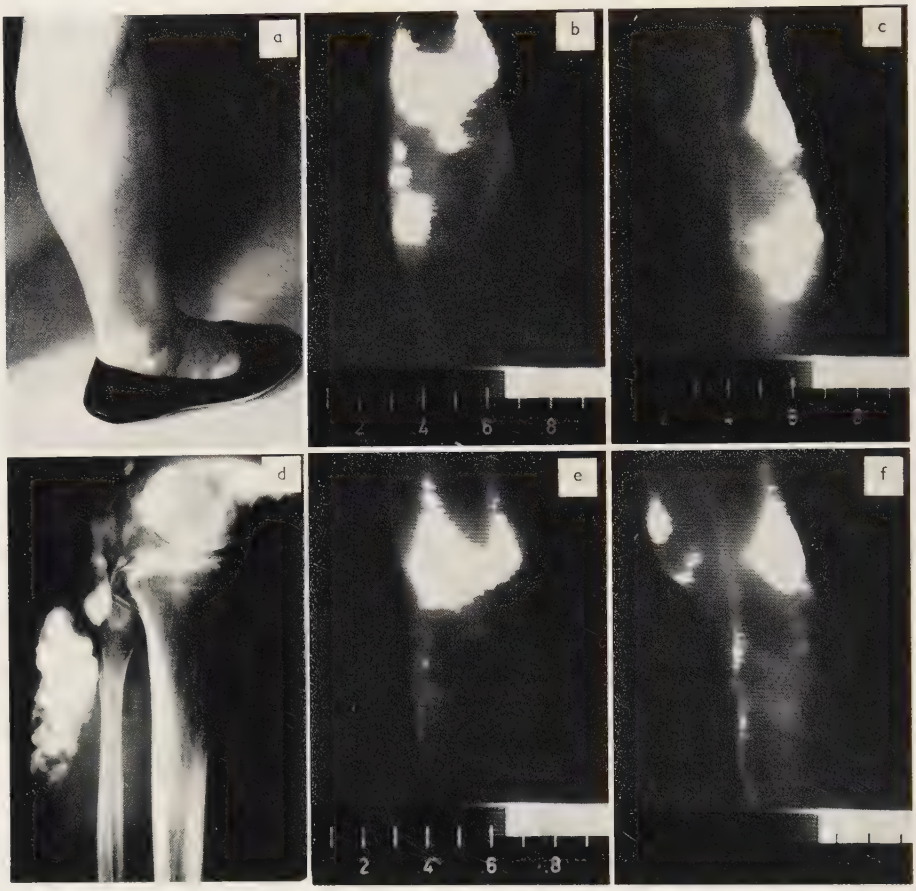


Fig. 26. Popliteal cyst in the right knee joint region of a patient with RA. (*a*) The cyst could easily be palpated in the calf; (*b*) heat emission pattern of the popliteal region shows temperature elevation over the cyst; (*c*) medial aspect of the corresponding area; (*d*) arthrography showed a large cyst communicating with the joint cavity; (*e*) and (*f*) illustrate the popliteal region one month after surgical removal of the cyst.

joints in RA. Four out of fifteen joints showed a satisfactory result with no thermographic evidence of inflammatory reaction after an observation time of between three and sixteen months. Heat emission patterns and clinical observations did not agree, however, for two joints (knee and shoulder). Despite the disappearence of palpable effusion in these joints, heat was still present, indicating inflammatory activity. Table 4 will give further information on fifteen joints in RA cases treated with radioactive gold. Serial scannings from two of the joints are illustrated in Figs. 24 and 25.

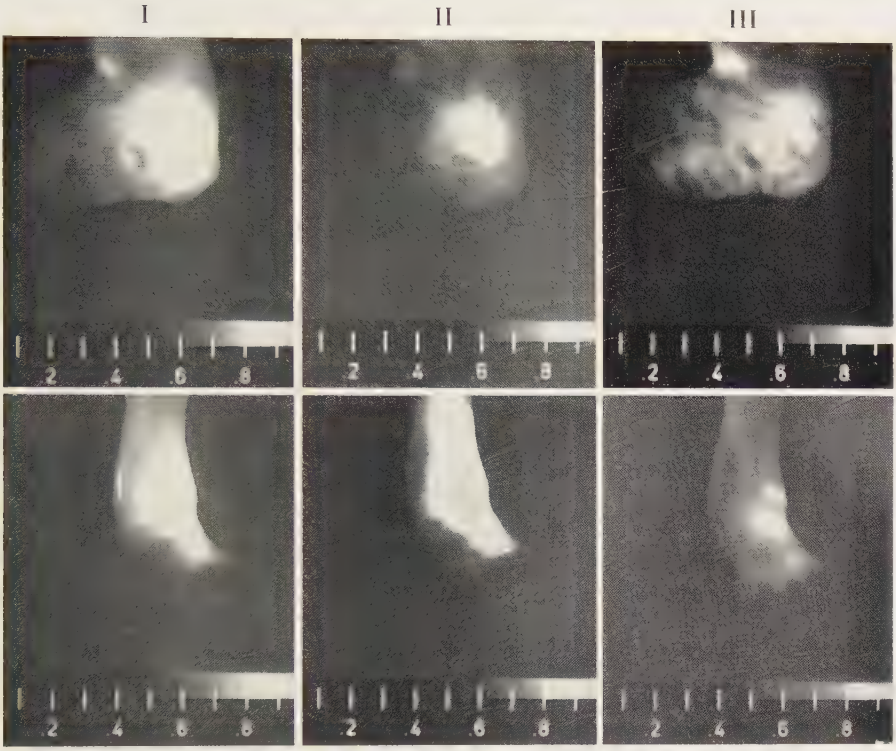


Fig. 27. Elbows and ankles of a patient with early RA treated with ACTH (Acton prolongatum Ferring, 24 IE three times a week). Scannings were made before treatment (I), after one week (II) and after two weeks of treatment (III).

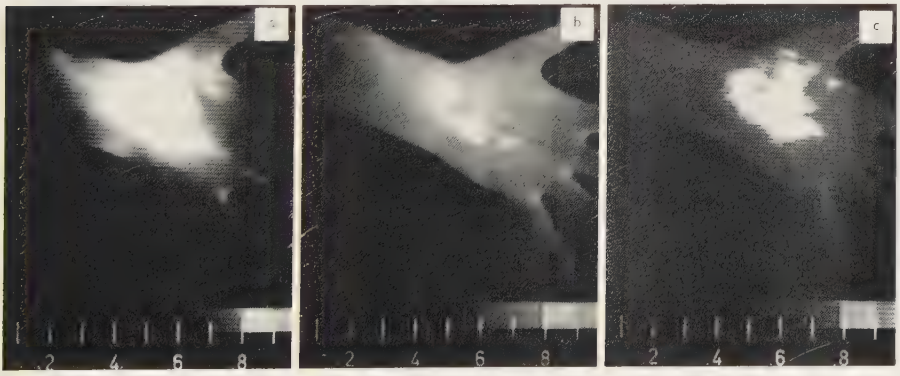


Fig. 28. Right wrist of a patient with an early RA treated with Prednisolone, 7.5 mg, daily. (*a*) Before treatment; (*b*) after three weeks; (*c*) after seven weeks of treatment an increase in heat emission has occurred although the dosage of the corticosteroid was kept unchanged.

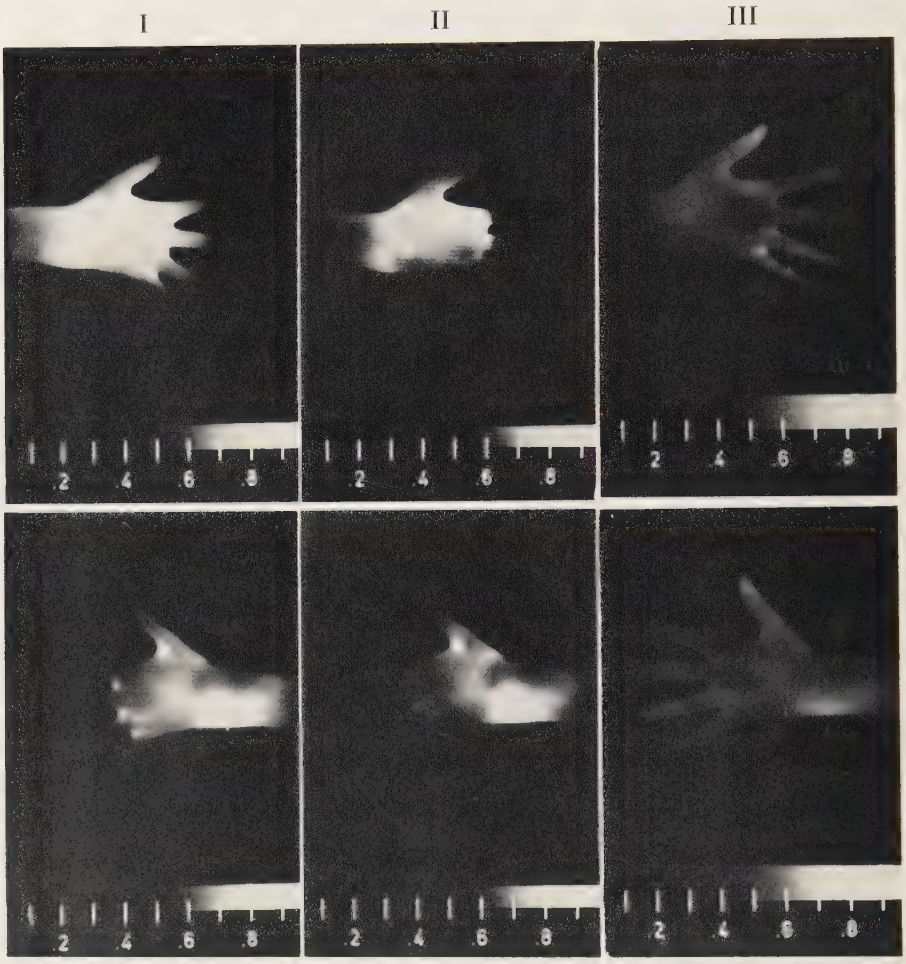


Fig. 29. Both hands of a patient with RA treated with Phenylbutazone (Butazolidin® alka Geigy) before (I) and after two weeks (II) on 0.3 g daily. Heat emission patterns reveal a marked decrease in the right second metacarpo-phalangeal region while the left caput ulnae region remains unchanged. Three months later (III) on the same dosage a definite improvement in both hands has occurred.

Removal of popliteal cyst

The thermal pattern of the calf region is well in accordance with the topographic distribution of the popliteal cyst as found by palpation and by arthrography (Fig. 26). Surgical removal is followed by a decrease in heat emission over the cyst region. The wall of the removed cyst in Fig. 26 showed chronic nonspecific inflammatory changes.[1]

[1] Department of Pathology, Regionsjukhuset, Örebro, Sweden.

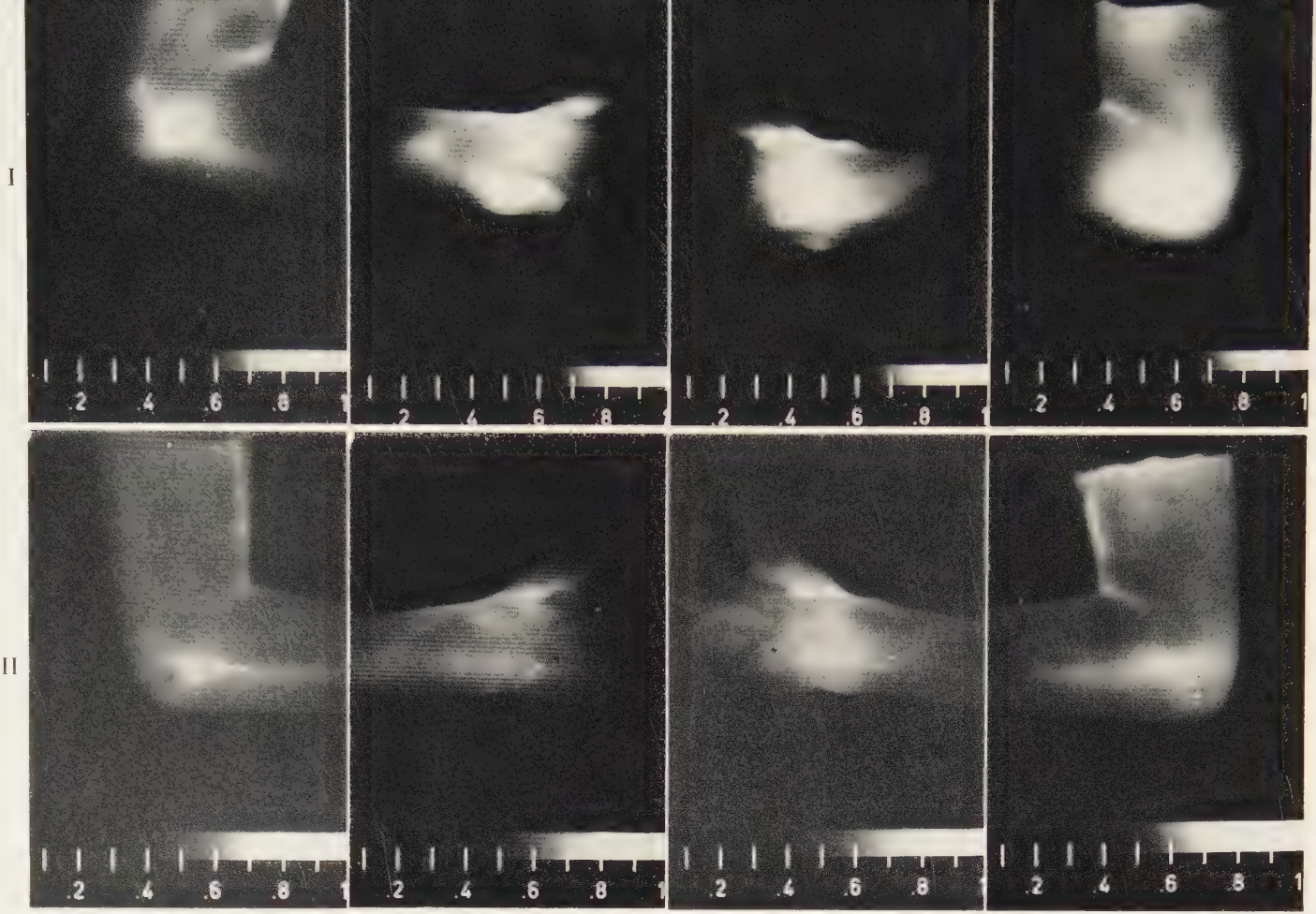


Fig. 30. Elbows and wrists of a patient with RA treated with Oxyphenylbutazone (Tanderil® Geigy) before (I) and after three weeks (II) on 0.6 g daily. A rapid improvement was noted with reduced heat emission.

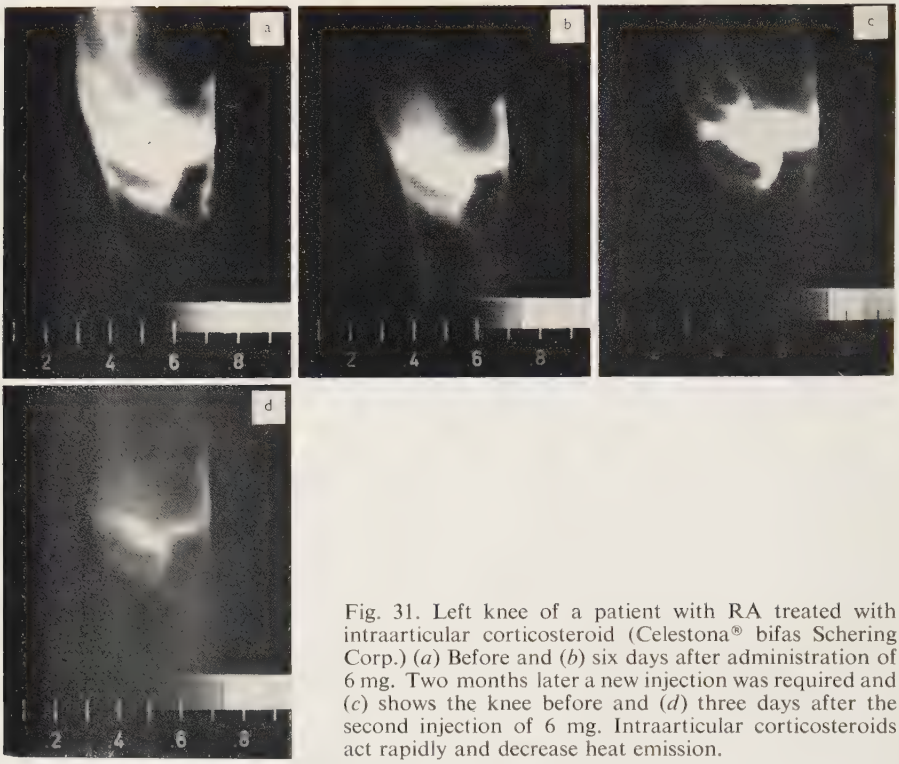


Fig. 31. Left knee of a patient with RA treated with intraarticular corticosteroid (Celestona® bifas Schering Corp.) (*a*) Before and (*b*) six days after administration of 6 mg. Two months later a new injection was required and (*c*) shows the knee before and (*d*) three days after the second injection of 6 mg. Intraarticular corticosteroids act rapidly and decrease heat emission.

Antirheumatic agents

The effect of ACTH, Prednisolone, Phenylbutazone, Oxyphenylbutazone and intraarticular corticosteroid on the heat emission from joints in RA is illustrated in Figs. 27–31. Comments are given in the legends. Changes in the emission patterns indicating improvement following treatment with these agents were present in all cases. The most rapid effect upon the joint temperature was obtained with intraarticular corticosteroid treatment.

COMMENTS

A thermogram is the registration of thermic events reflecting deep and superficial circulatory mechanisms as well as tissue metabolism modified by the condition of the overlying skin and nervous and circulatory communications. An experimental evaluation of factors controlling the patterns of the infrared emission as recorded by IRT has been made by Brånemark & Nilsson (1969), who also gave consideration to modifications of the original emission signal during processing within the recording instrument. They concluded that a quan-

titative evaluation of biological phenomena by registration of infrared emission should be based on the biophysical fact that the temperature at a surface is the result of the contribution of heat from blood and tissue metabolism conducted through interposed tissues, directly or via the vascular system, and from incident radiant energy. The actual surface temperature as registered by emission recording as radiant heat is, however, modified by heat flux through conduction and convection and heat flux through evaporation.

A great advantage of the infrared camera used in the present study is the isotherm function which makes densitometric measurements of the thermograms unnecessary. The emission picture of superimposed isotherms provides simple and fast analysis automatically included in the original document of the inflammatory process. It is thus possible to produce clinical records which may be compared over long periods of time. Working exclusively with isotherms, as in the present study, makes choice of film material, exposure time and processing technique less important, factors that are of the utmost relevance in densitometric evaluations of thermograms. Grading surfaces by means of planimetry according to the above mentioned method in the author's opinion works satisfactorily if a numerical value of the intensity of the inflammatory process is required. In clinical routine work, however, a direct ocular examination of the thermal picture regarding distribution and area of isotherms seems to be a practical and sensitive enough procedure for information about the disease condition.

A temperature reference with constant temperature and emissivity and hence with a known radiation output is essential for comparative thermography of inflammatory conditions when judging therapeutic effects and variations in the local disease activity. Such thermal reference sources are available commercially[1] but the water bath used in the present study has worked quite satisfactorily. It has been necessary to calibrate the infrared camera several times during prolonged use against the reference source because the camera might need several hours (Nilsson, 1969) to reach more stable scanning properties although it probably never reaches complete stability. It must again be stressed that the reference temperature of 28.3 C cannot automatically be transferred into absolute degrees thus making exact skin temperature measurements possible. It only serves as a constant reference (obtained by adjusting the thermometer of the water bath to 28.0 C) to which temperature differences may be related. In clinical evaluation work it is the temperature difference rather than the absolute temperature that is of prime interest.

Some authors (e.g., Haberman, Ehrlich & Levenson, 1968) prefer to relate the thermal pattern of the joints involved with the pattern of adjacent regions of

[1] AGA, Lindingö 1, Sweden.

the limb in order to estimate the temperature difference between the two regions and to use the latter as a reference. They claim, however, that even in muscles of patients with RA prominent hot spots indicating the presence of focal myositis were detected particularly during active phases of the disease. Furthermore it must be remembered that quantitation of the temperature difference between two different areas of skin obtained by means of IRT requires constant and equal emissivity for both areas. These facts support the opinion that a reference outside the body which is not influenced by local variations in the tissue temperature or the skin emissivity appears to be safer in comparative thermography.

Joint temperature elevation in connection with physical exercise of adjacent muscle groups has been discussed by Harris (1963), who found that the clearance of radioactive sodium from the knee joint was significantly raised following muscular exercise indicating an increase in local blood circulation within the synovial cavity. Hollander & Horvath (1949) also found an elevation in intraarticular temperature in connection with active weight-bearing movements. In two normal subjects a mean temperature increase of 2.3°C was observed. It is less probable that increased joint friction would cause the rise in heat production since Wright & Johns (1961) pointed out that only in severely damaged joints with marked clinical and radiological deterioration could friction be demonstrated (second metacarpo-phalangeal joint). The patient illustrated in Fig. 21 had normal knee radiograms. It is, however, generally assumed that the average case of RA can tolerate a programme of resistance exercises without local flare-up if judiciously handled (Bowie, 1964).

Hypervascularisation in the incision and wound healing phenomena probably contribute to sustained heat production despite local well-being following surgical synovectomy in some patients. It is felt that a minimum of six months postoperatively is required before any definite conclusions about the result can be drawn using IRT.

IRT as a tool in evaluating results of synovectomy of finger joints might be hazardous. Asymmetric findings common in rheumatoid hands cannot be relied upon as a diagnostic sign because there are variations which must be considered to lie within the normal range (Brånemark, 1967).

The fifteen joints treated with colloidal radioactive gold that are reported in this study were selected from a larger patient group with RA receiving this form of therapy. It is very difficult to avoid other forms of treatment during a sufficiently prolonged observation time following intraarticular administration of antirheumatic agents. In these fifteen joints with effusion, however, no other major change in the treatment programme was undertaken during the follow-up period. Six out of fifteen joints showed satisfactory results with no evidence of palpable hydrops, heat emission remaining unchanged, however, in two of the joints. This might indicate a transitory radiation effect upon the exudate-

producing cells of the synovial membrane while deeper parts of the joint capsule are not influenced by this form of treatment. The remaining nine joints all relapsed within six to twelve months. The distribution of radioactivity within different depths of the knee joint capsule has shown a relative activity per gram tissue of 110 in the synovial lining cells as compared to 22 in the remaining capsule layer and there is probably a steep activity gradient within the synovial layer (Gynning, Odelberg-Johnsson, Waldeskog & Wendeberg, 1965). Beta radiation is absorbed to a depth of about one millimeter and approximately 90 per cent of the tissue changes and therapeutic effect of radioactive gold results from such surface absorption (Virkkunen, Krusius & Heiskanen, 1967).

Hollander, Stoner, Brown & deMoor (1951) reported on a pronounced fall in joint temperature (measured with a thermocouple introduced into the joint cavity) within the first twenty-four hours after parenterally administered ACTH or cortisone. They suggested serial joint temperature determinations as a method for evaluation of therapeutic effectiveness of anti-arthritic agents. The findings in the present study are in agreement with their results. The most rapid decrease in joint temperature was caused by intraarticular administration of corticosteroids, a finding that has been reported several times before in the literature (e.g., Hollander et al., 1951, Gershon-Cohen, Haberman-Brueschke & Brueschke, 1965).

In order to secure stable scanning properties in the recording instrument it is important to have the joint in question projected centrally on the oscilloscope screen and in case of serial scannings always to try to locate it in the same area of the screen. There is evidence that different parts of the screen shows different sensitivity (Nilsson, 1969). Another problem with the infrared camera used is the prolonged warming up time required until temperature drift ceases. A drift of 12°C during the first three hours has been reported and Nilsson (1969) maintains that the camera probably never reaches completely stable properties. Frequent calibration controls as described above will reduce this error in the recording procedure. The influence of the focusing distance upon the sensitivity has been studied by Borg (1967) and was found to be significant at a distance measured from the spherical mirror to the object of between 2.3 and 6 meters. It is therefore important to keep the focusing distance as constant as possible in serial scannings.

CONCLUSION

It is concluded that IRT is a valuable method for evaluating the inflammatory activity of joints in RA *provided* that the following precautions are observed.

Minimize the influence of changes in peripheral circulation in the patient

in connection with smoking or heavy meals and try to keep a constant room temperature of between 18° to 20°C during scanning.

Minimize the effect upon the heat emission signal produced by unstable properties in the recording instrument by trying to keep a constant distance between the patient and the camera, by trying to locate the joint as centrally as possible on the oscilloscope screen and by performing frequent calibration controls against a constant infrared radiation reference source during prolonged use of the camera for temperature drift compensation.

If these precautions cannot be observed the use of IRT in evaluating local inflammatory activity in RA over different periods of time may produce false records of the local disease process.

Chapter 2

ON THE RELATION BETWEEN HEAT EMISSION, WHITE BLOOD CELL COUNT AND LACTIC DEHYDROGENASE ISOENZYME CONTENT IN RHEUMATOID KNEE JOINTS WITH EFFUSION

A decrease in joint temperature measured by IRT following intraarticular administration of corticosteroids to inflamed joints in patients with RA has been demonstrated earlier in this investigation (Chapter 1). The reduced infrared radiation from the joint following this form of therapy was interpreted to be due to an antiinflammatory effect caused by the drug and the emission thus served as an activity parameter of local joint inflammation.

Among others, Furey, Clark & Brine (1959) have pointed out that the degree of inflammatory activity in the rheumatoid arthritic joint is reflected in the white blood cell (WBC) count of the synovial fluid.

Studies by Alexandersson, Nettelbladt & Sundblad (1968) showing that the lactic dehydrogenase (LDH) isoenzyme content in arthritic synovial fluid decreased markedly following intraarticular administration of corticosteroid, suggest that alterations in the LDH content, especially LDH 5, are related to the local joint inflammatory activity.

Thus three different methods apparently could be used to measure local joint disease activity in rheumatoid arthritic joints, one clinical (IRT) and two laboratory tests (WBC count and LDH 5 isoenzyme content in synovial fluid). It was therefore considered of interest to study whether there exists any parallelism between changes in these parameters of inflammatory activity. Sufficient evidence seems to exist indicating that IRT measures local disease activity in RA (Chapter 1). Besides Furey et al. (1959), extensive studies by Ropes & Bauer (1953) have shown that the synovial WBC count is related to the clinical activity of joint inflammation in RA. However, no other study besides that of Alexandersson et al. (1968) has been found concerning the effect of corticosteroids on the LDH isoenzyme content and the significance of this parameter as an activity test requires further investigation.

Table 5. *Clinical and laboratory data on 19 cases of RA.*

Classification ...	"Classical" RA	"Definite" RA	"Classical" RA/ "Definite" RA
Number of cases	11	8	
Females	6	6	
Males	5	2	
Average age (years)			
Females			52.6
Males			55.4
Average duration of arthritis (years)			
Females	15.3	15.5	
Males	10.4	10.5	
Stage			
I	0	8	
II	7	0	
III	4	0	
IV	0	0	
Pos SSCA	11	2	

MATERIAL AND METHODS

Nineteen patients with RA admitted to the Department of Rheumatology, Regionsjukhuset, Örebro were included in the study. "Classical" and "definite" cases of RA according to the American Rheumatism Association criteria (1958) were studied.

"Classical" RA: 11 patients, 6 females and 5 males. Rheumatoid progression according to Steinbrocker et al. (1949): 7 patients were in stage II and 4 in stage III.

"Definite" RA: 8 patients, 6 females and 2 males. 8 patients were in stage I.

The mean age in the female group was 52.6 years, in the male group 55.4 years. The average duration of the disease was 15.3 years for "classical" females, 15.5 years for "definite" females, 10.4 years for "classical" males and 10.5 years for "definite" males. Table 5 shows some clinical and laboratory data on the nineteen patients with RA.

Heat emission from the arthritic joints was measured by means of IRT according to the method described earlier (Chapter 1) and the thermograms were quantitated in heat counts according to method II.

WBC counts on the synovial fluid were performed according to the method described by Ropes & Bauer (1953) using a Bürker chamber with a sodium chloride solution as diluent.

The LDH isoenzyme content of the synovial fluid was determined according to the method described by Alexandersson et al. (1968).[1]

[1] Doc. Lars Sundblad, Central Clinical Laboratory, Södersjukhuset, Stockholm, Sweden.

Table 6. *Values for heat count, WBC count and LDH 5 content simultaneously obtained at first and second examination of knee joints in patients with RA.*

Total LDH values are given in brackets. Paired observation numbers 1–17 constitute non-synovectomized and 18–25 synovectomized joints. In one case (No. 23) a synovectomy was performed immediately after the first examination. No. 25 was synovectomized eighteen months before the first examination. Two joints (Nos. 1 and 4) had received radioactive gold twelve and six months, respectively, before the first examination.

Paired observation number	Heat counts (arbitrary units) examination		WBC counts (cells/cu. mm.) examination		LDH 5 (units/ml) total LDH in brackets examination		Time interval between I and II days
	I	II	I	II	I	II	
	Nonsynovectomized joints						
1	64	6	7,000	320	343 (1000)	280 (778)	60
2	108	0	11,400	5,000	215 (720)	131 (535)	45
3	56	10	27,000	260	332 (1012)	85 (320)	45
4	40	544	14,400	18,200	587 (1760)	714 (2000)	60
5	58	184	10,000	16,400	57 (283)	150 (500)	60
6	172	12	8,600	4,000	425 (1175)	161 (455)	60
7	312	280	16,400	13,000	508 (1388)	542 (1644)	6
8	52	0	5,000	1,800	150 (477)	114 (410)	3
9	296	178	21,100	12,000	326 (944)	240 (755)	6
10	352	166	18,000	12,800	694 (2000)	736 (2165)	75
11	288	68	13,400	10,200	436 (1388)	341 (1110)	15
12	16	54	400	3,200	498 (1088)	684 (1665)	45
13	150	0	400	400	116 (388)	70 (255)	3
14	114	0	200	200	55 (244)	39 (201)	6
15	0	36	1,800	4,600	114 (410)	151 (555)	75
16	178	240	12,000	17,200	240 (1755)	438 (1270)	60
17	0	214	400	400	70 (255)	45 (320)	15
	Synovectomized joints						
18	285	228	20,600	16,800	453 (1550)	566 (1933)	60
19	266	46	68,000	200	217 (616)	261 (666)	60
20	284	18	16,800	16,400	562 (1540)	577 (1778)	60
21	62	114	1,200	0	112 (350)	111 (333)	60
22	136	22	12,000	4,200	153 (555)	179 (600)	3
23	316	226	13,600	9,700	452 (1250)	191 (544)	75
24	22	58	4,200	8,400	179 (600)	111 (377)	75
25	62	216	7,100	10,000	272 (833)	376 (930)	75

The coefficient of concordance in the changes of two variables between two different points of time has been measured with the phi-coefficient (Baggaley, 1964). In this case the phi-coefficient indicates to what degree the changes are correlated when only their direction have been registered.

Synovial fluids were aspirated with sterile precautions from the knee joints without using local anaesthetics. Infrared scanning was always carried out before aspiration. In six patients both knees were studied and a total number of twenty-five joints were measured, twenty on two and five on three different occasions at different intervals. Nine joints had been synovectomized four to

Table 7. *Coefficients of concordance between heat counts and WBC counts or heat counts and LDH 5 content in nonsynovectomized and synovectomized joints in patients with RA.*

	Number of paired observations	Φ (Heat count; WBC)	Φ (Heat count; LDH 5)
Non synovectomized joints	17	0.63 ($P<0.01$)	0.63 ($P<0.01$)
Synovectomized joints	8	0.75 ($P<0.05$)	−0.47
Whole material	25	0.65 ($P<0.01$)	0.28

eighteen months before the first examination and two had received colloidal radioactive gold six and twelve months, respectively, before the first examination. Two joints were synovectomized between the first and the second examination.

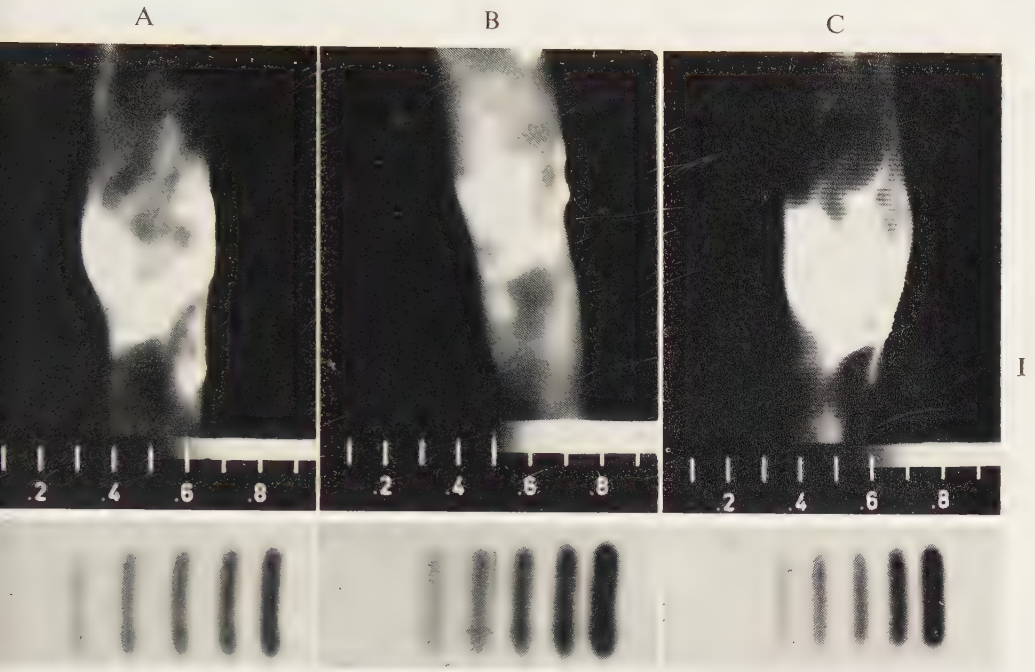
RESULTS

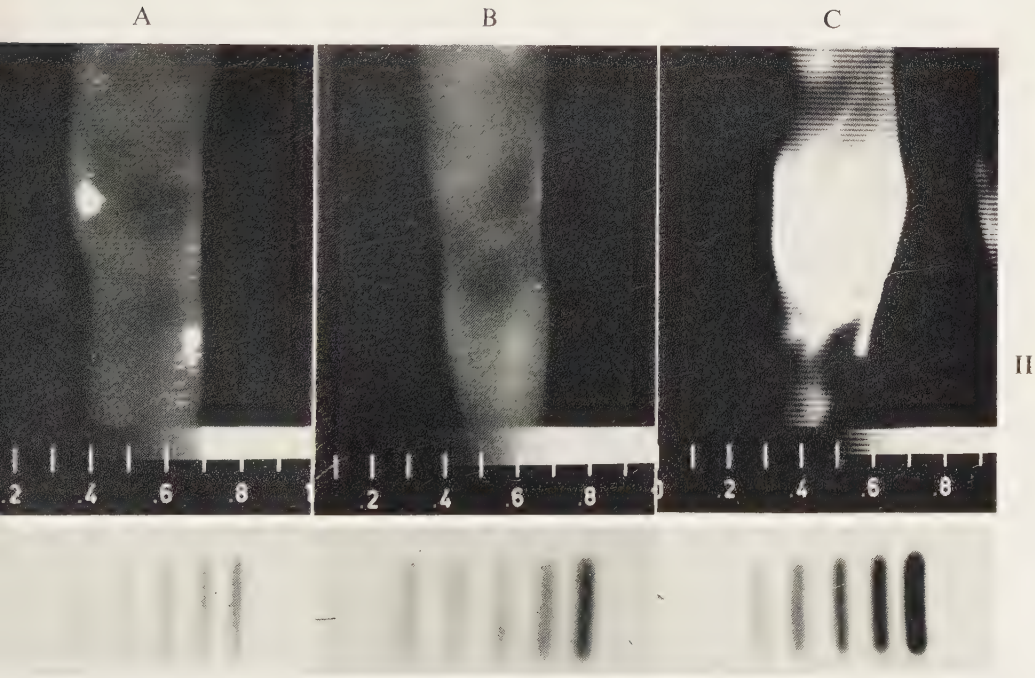
Table 6 shows the values for heat count, WBC count and LDH 5 content simultaneously obtained at different occasions with varying intervals. Table 7 gives the coefficients of concordance between the different variables. A significant concordance ($P<0.01$) was found between heat counts and WBC counts as well as heat counts and LDH 5 content in nonsynovectomized knee joints. In synovectomized joints, however, a less significant concordance ($P<0.05$) was obtained between heat counts and WBC counts while no concordance could be demonstrated between heat counts and LDH 5 content. For the whole material a significant concordance ($P<0.01$) was found between heat counts and WBC counts. The correlation coefficient between WBC counts and LDH 5 values was $r=0.62$.

Fig. 32. Three paired observations of heat emission from knee joints in patients with RA and LDH zymograms of corresponding synovial fluids.

	I			II		
	Heat count (Arbitrary units)	LDH 5 (units/ml)	Total LDH (units/ml)	Heat count (arbitrary units)	LDH 5 (units/ml)	Total LDH (units/ml)
A	172	425	1 175	12	161	455
B	108	215	720	0	131	535
C	312	508	1 388	280	542	1 644

Time interval A I–II 60 days, B I–II 45 days, C I–II 6 days.


A
B
C
.2
.4
.6
.8
I


A
B
C
.2
.4
.6
.8
II

In Fig. 32 three paired observations of heat emission from knee joints in patients with RA and LDH zymograms of corresponding synovial fluids are shown.

COMMENTS

The findings in this study indicate that a definite relation would seem to exist between heat emission obtained by IRT and the WBC count from synovial fluid in both nonsynovectomized and synovectomized knee joints with effusion due to RA.

There apparently also exists some parallelism between heat counts and the LDH 5 content in nonsynovectomized joints, although the differences in LDH 5 values in many cases are too small to allow definite conclusions. It should be pointed out in this context that attempts to provoke a more rapid and considerable decrease in the LDH content using intraarticular corticosteroids, as in the study by Alexandersson et al. (1968), were made only in a few cases and often resulted in a complete disappearence of the effusion by the second examination. In the majority of observations, however, the time interval between the first and the second examination was between 1.5 to 2.5 months and during this time the effect upon LDH formation produced by the steroid might well have been abolished. So in fact most of the observations were performed on knee joints with spontaneous fluctuations in local inflammatory activity and this might explain the small differences in LDH 5 content appearing in many cases.

The source of the elevated LDH content in the synovial fluid of inflamed joints in RA is probably the altered synovial tissue. Hamerman & Blum (1959) reported that the synovial lining cells are rich in LDH and Alexandersson et al. (1968) found very high amounts of LDH 5 in proliferative synovial tissue obtained in connection with synovectomy performed on patients with active RA. The elevated isoenzyme content probably indicates a very high metabolic activity in the lining cells. West, Poske, Black, Pilz & Zimmerman (1963), however, found a positive correlation between the WBC count in the synovial fluid and LDH activity, and they considered this as indirect evidence of the release of enzymes from the white cells. Cohen (1964) demonstrated a positive correlation ($r=0.62$) between the WBC count and LDH content whereas Vesell, Osterland, Bearn & Kunkel (1962) and Alexandersson et al. (1968) noted that the elevation of LDH activity was not proportional to the number of white cells observed in synovial fluids from rheumatoid joints.

If a difference exists in the relation between changes in heat emission and the LDH 5 content in nonsynovectomized and synovectomized joints, as this study might indicate, it is tempting to speculate on the possibility that this could be due to alterations in the synovial tissue during the first year after synovectomy. The removal of rheumatoid granulation tissue in connection with synovectomy

might disturb the synthesis of LDH isoenzymes in the synovial lining cells. Synovectomy immediately after the first examination (Observation 23, Table 6) might in this case have contributed to the marked decrease in LDH 5 two and a half months later while wound healing phenomena still caused the temperature elevation as measured by IRT. Eighteen months after synovectomy (Observation No. 25, Table 6) the synovial tissue with its original metabolic properties could have regenerated completely and the relation between heat emission and LDH 5 resembles that found in the majority of nonsynovectomized cases. Goldie (1969) has demonstrated macroscopically as well as microscopically areas of tissues in the rheumatoid joint with pathomorphologic changes similar to the original findings in twenty-seven joints up to one year after synovectomy. Two joints in the present material (Observations 1 and 4, Table 6) had been treated with radioactive gold twelve and six months, respectively, before the first examination and they both behaved like nonsynovectomized joints as regards the relation between heat emission and the LDH 5 content. This might indicate a transitory effect caused by the beta radiation upon the synovial lining cells with proportionately rapid regeneration of their metabolic properties.

CONCLUSION

It is concluded that unidirectional changes occur in heat emission, WBC count and LDH 5 isoenzyme content during spontaneous fluctuations in local joint disease activity in nonsynovectomized rheumatic knee joints with effusion. Proportionately small changes occur, however, in LDH 5 activity and it seems safer to use WBC counts of the synovial fluid as a laboratory test of local joint disease activity when compared with clinical activity estimation using IRT. As regards changes in total LDH compared with changes in LDH 5, no advantage has been found in favour of the latter as a measure of local activity.

Chapter 3

JOINT STIFFNESS DETERMINATIONS IN RHEUMATOID ARTHRITIS

Joint stiffness is an important manifestation in RA and especially morning stiffness appears to be a very characteristic symptom in active periods of the disease. It heads the list of diagnostic criteria for RA proposed by the American Rheumatism Association (1958) and the duration of morning stiffness has been used by Lansbury (1958), among others, as a systemic disease activity parameter.

Wright (1959) measured the strength of grip in patients with RA throughout the day and found a marked weakness in the morning and suggested that the patient might experience stiffness when the strength of grip falls below a critical level. Scott (1960) used an extension spring in estimating stiffness in the second metacarpo-phalangeal (MP) joint and found a marked diurnal variation in patients with RA.

Wright & Johns (1960*a*) described a method whereby joint stiffness in the second MP joint could be measured in precise physical terms. They used a heavy pendulum that imposed a sinusoidal rotary motion upon the joint and recorded the torque required to impose this motion with strain gauges. They later replaced the pendulum with a variable speed motor and the apparatus was called the arthrograph. Using this, they have studied joint stiffness in normal and diseased joints as well as in other forms of connective tissue and neuromuscluar disorders (Wright & Johns, 1960*b*, 1961). The relative importance of various tissues in joint stiffness has also been discussed (Johns & Wright, 1962). Further work by these authors has been summarized by Wright & Plunkett (1966).

Long, Thomas & Crochetiere (1964*a*, 1964*b*, 1965) used a modified arthrograph in studying muscle tone in the hand and they concluded that the method provides a useful tool for the evaluation of drug effects in conditions of spasticity or rigidity. The resistance offered by the third MP joint is measured by this mehod and studies were performed in normal subjects as well as in patients with spastic hemiplegia.

A simple method of measuring joint stiffness in the hand was described by Rice (1967). He used a pendulum attached to the middle finger and imposed a motion upon the third proximal interphalangeal (PIP) joint. The damping rate caused by the resistance in the joint was registered.

Ingpen & Hume-Kendall (1968) measured joint stiffness in MP joints by a

dynamic method by means of timing a 10-degree free fall at the joint and found quantitative reduction in stiffness following "warming-up" exercises and wax baths.

Hicklin, Wighton & Robinson (1968) also measured stiffness in MP joints using the free fall time technique.

Using the arthrograph described by Wright & Johns (1960) with slight modifications, Bäcklund & Tiselius (1967) found this method useful in the clinical assessment of stiffness in patients with digital RA in Steinbrocker stages I and II. The method could be applied also in patients with a more advanced stage of the disease provided that ulnar deviation or volar subluxation of the MP joints was only mild and did not prevent joint motion to any considerable degree. Aquilonius & Tiselius (1969) also applied the method for rigidity registrations in patients with Parkinson's disease.

The aim of this study was to collect further clinical experience of joint stiffness determinations in the evaluative work concerning patients with digital RA. The following main problems concerning stiffness in MP joints will be discussed:

Stiffness in normal joints.
Stiffness in arthritic joints with special reference to
- temperature influence upon stiffness in arthritic joints,
- morning stiffness (difference between morning and afternoon values),
- relation to hand volume and gripping strength,
- relation to systemic disease activity,
- relation to rheumatoid changes in the joint,
- relation to rheumatoid changes in flexor and extensor tendons.

METHODS

A simplified model of the apparatus described in detail by Wright & Johns (1960 *b*) was used.

A rotational sinusoidal motion is imposed upon the second MP joint. The motion is produced by a variable speed motor and the amplitude of rotation of the joint can be varied from 0° to 70° to 17° to 47° flexion. The rotational velocity can also be varied. Strain gauges mounted on the lever which transmits the motion from the shaft to the finger record the amount of resistance the finger is offering against the passive sine wave motion. By recording simultaneously from the strain gauges and the driving device, plots are obtained from the position of the finger and the resultant torque resisting the movement. Position and torque are recorded simultaneously on a Tektronix Model 502 A dual-beam oscilloscope with a polaroid attachment. Fig. 33 illustrates the technical arrangements. In Fig. 34 typical slopes recorded bilaterally from normal MP joints are shown. The instrument was calibrated with weights and showed a linear rela-

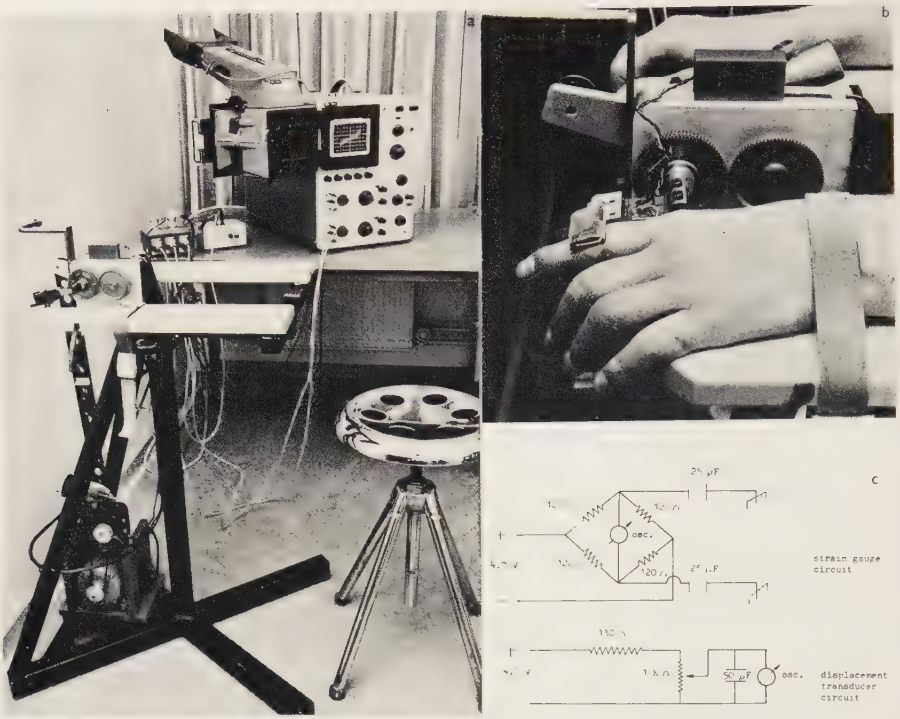


Fig. 33.(*a*) The joint stiffness device consists of a variable speed motor that imposes a sinusoidal motion upon the second MP joint. Strain gauges record the resistance offered by the finger, and torque versus deformation (displacement) is plotted on an oscilloscope screen. (*b*) Left index finger attached to the apparatus. (*c*) Strain gauge and displacement transducer circuit, for further explanation see text.

tion between applied weights and torque amplitude on the oscilloscope screen. Great care must be taken in aligning the axis of rotation of the joint and the apparatus which is facilitated by the centre indicator. The equipment gives a varying speed of movement during a cycle, maximum speed being obtained at midpoint (displacement - zero). At the end-points $\pm 35^{\circ}$ to $\pm 15^{\circ}$ deformation, speed reverses and the force/deformation ratio approximates elastic stiffness. At the midpoint, on the other hand, plastic yield and viscosity may be significant as also suggested by the degree of hysteresis in the slope at this point. To get a stabilized power supply to the strain gauge circuit and the displacement transducer circuit the 220 volt mains AC was transformed and rectified. The stabilizing effect was obtained through a zener diode giving an output of 4.7 volts at a maximum current of 75 mA.

Calculation of joint stiffness in the MP joints can be made with regard to end-point and mid-point stiffness (Bäcklund & Tiselius, 1967). In this case an oscilloscope sensitivity of 0.2 mV per cm on the vertical axis and 1.0 mV per

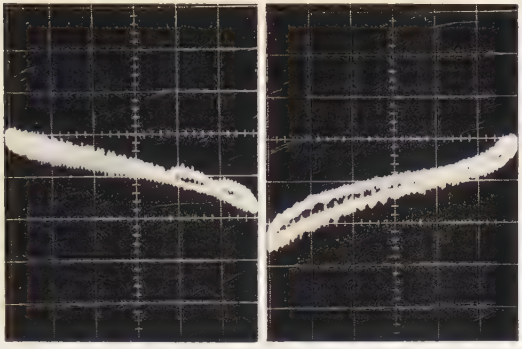


Fig. 34. Stiffness slopes from normal MP joints. Torque on the vertical axis and displacement on the horizontal axis. (*a*) Left and (*b*) right second MP joint.

cm on the horizontal axis was used. Joint stiffness was calculated from the slopes and expressed in kpcm per radian. Measurements from a series of twelve records taken when the hand was removed from the apparatus and then replaced again showed a maximum deviation of 3.5 per cent of the mean value at flexion and 1.7 per cent of the mean value at extension.

Using this method in clinical routine work, however, it soon became apparent that calculation of joint stiffness according to the initial method outlined above (Bäcklund & Tiselius, 1967), although a sensitive method of calculating stiffness in precise physical terms, could be simplified. No further important clinical information was obtained by making a distinction between end-point and mid-point stiffness. On the contrary, more attention has been paid to the varying degrees of hysteresis in the stiffness slopes, a phenomenon that appeared in some cases very clearly by decreasing the rotational velocity from the initially used 1.0 cycle per second (c/s) to 0.33 c/s. Thus some modifications were undertaken as compared to the initial method in the clinical routine work evaluating joint stiffness in patients with RA.

The modified method used in the present investigation utilizes a rotational velocity of 0.33 c/s and an amplitude of rotation in most joints of $\pm 30^{\circ}$, mid-point at 35° flexion. Bilateral registrations in MP joints of the index finger. Quantitative measures used include peak-to-peak torque in Newton units (N) and the hysteresis phenomenon as an indication of certain energy losses in the system which was measured by determination of the area of the slope with a planimeter and expressed in Newton cm per cycle (Ncm/c).[1] Fig. 35 illustrates the calculation of peak torques and planimetric area in three bilateral registrations of joint stiffness in arthritic MP joints. The torques observed on the vertical axis were converted into N by using a calibration curve. In most

[1] Joint stiffness in reality constitutes a torque but is expressed in Newton units when the lever of the apparatus is constant (5.0 cm).

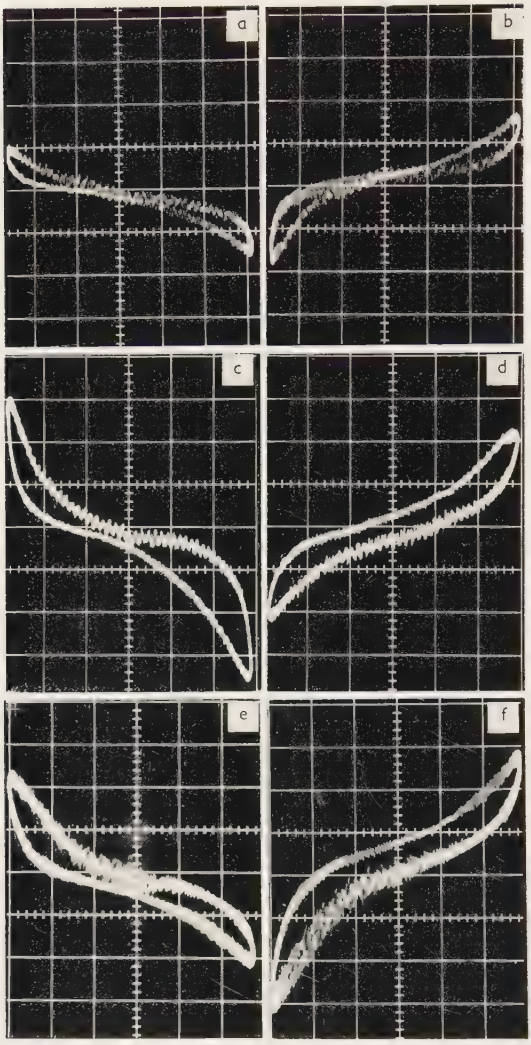


Fig. 35. Stiffness slopes from rheumatoid arthritic MP joints. Certain basic types of data were reduced including (1) *Peak-to-peak torque*. This torque was measured from peak to peak seen in the extremes of range (at 5° and 65° flexion) and it represents primarily elastic forces and is converted into Newton units by using a calibration curve. (2) *Planimetric area* within the slope. This area was measured using a planimeter. With appropriate scales the area was converted into Newton centimeters per cycle. The area represents energy loss and relates primarily to viscosity. If there were no losses in the system, the slope would be a line (pure elastic system) and would have no area. Elastic factors relate to position while viscous factors relate to velocity.

	Peak-to-peak torque (N)	Planimetric area (Ncm/c)
a	2.45	1.65
b	3.43	1.78
c	6.47	4.44
d	4.41	3.67
e	4.51	3.50
f	5.97	4.99

cases a sensitivity of 0.2 mV/cm was used where one cm of displacement corresponds to 0.98 N. In very stiff cases the sensitivity was diminished to 0.5 mV/cm where the same displacement corresponds to 2.55 N.

As has been pointed out earlier (Wright & Johns, 1960*a*; Bäcklund & Tiselius, 1967) no evidence has been found that muscle activity plays any part in the production of stiffness measured at the joint. Voluntary muscular contractions resisting the motion of the finger due to insufficient muscle relaxation during a slope registration can be detected because they produce distorsions in the tracing (Fig. 36). In order to further study whether there is neural control

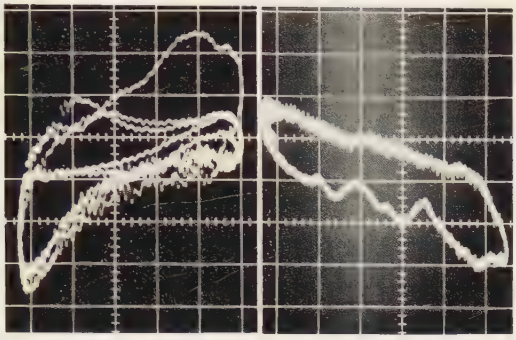


Fig. 36. Distorsions in the slope due to insufficient muscle relaxation.

of the muscle tone in the hand during stiffness registrations using the method outlined above and whether such control contributes in any degree to stiffness the following experiments were made.

Electromyographic signals were monitored from the extensor and flexor muscles of the index finger during stiffness registration in two patients with active RA.[1] A 3-channel DISA electromyograph with concentric needle electrodes was used. During flexion in one case pain-induced distorsions in the tracing were accompanied by slight electromyographic activity in the extensor muscle, in other cases the absence of such activity indicated that the muscles were not contracting during the joint motion using 0.33 c/s (Fig. 37).

Joint stiffness registrations were made in seven patients with active RA before and after local axillary block anaesthesia using 20 ml 2 % Carbocain® – Adrenalin solution[2] in connection with hand surgery.[3] In one of the patients a slight decrease in the peak torque of the stiffness slope was noted, in the remaining six patients no change or a slight increase in the torque appeared after anaesthesia (Fig. 38). The patient that showed a slight decrease had a certain degree of ulnar deviation in her second right MP joint which sometimes makes it difficult to obtain reproducable stiffness tracings. Pain during motion in one case produced distorsions in the tracing that disappeared after anaesthesia while no change in the peak torque was noted.

To summarize, no active contraction of muscles contributes to stiffness in the second MP joint without being discovered by distorsions in the tracing. Pain-induced contractions are, however, seen occasionally. No evidence has been found that muscle tone in the hand give rise to alterations in the stiffness torque through neural control.

Local disease activity in MP joints was measured by means of infrared thermography according to the method outlined in Chapter 1.

[1] Dr. K.-G. Rignér, Department of Rehab. Med., Central Hosp., Ekilstuna.
[2] Dr. Rosander, Department of Anaesthesiology, Central Hosp., Eskilstuna.
[3] Dr. W. Aschan, Department of Orthopedic Surgery, Central Hosp., Eskilstuna.

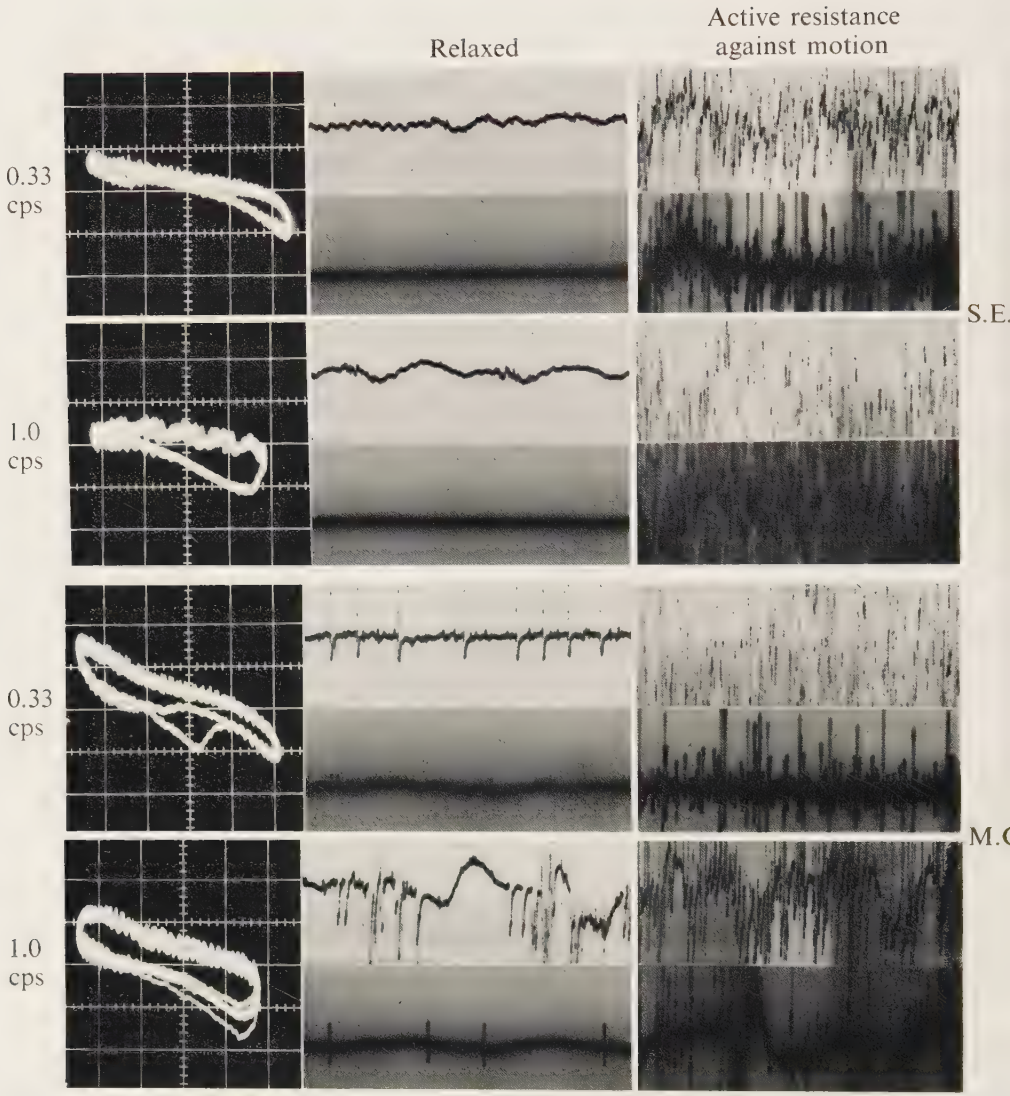


Fig. 37. EMG signals monitored from extensor and flexor muscles of the index finger in two patients with RA at two different rotational velocities. Distorsions in the slope due to pain on motion in one of the cases (M.G) were accompanied by slight EMG activity at 0.33 c/s, otherwise no EMG activity was found at this velocity. At higher velocities a stretch reflex might also be initiated.

Systemic disease activity was measured by three methods, viz., erythrocyte sedimentation rate (ESR), orosomucoid content in serum (Nettelbladt & Sundblad, 1962) and α_2-globulin content in serum. *ESR* was measured according to Westergren. *Orosomucoid content* was measured using paper electrophoresis

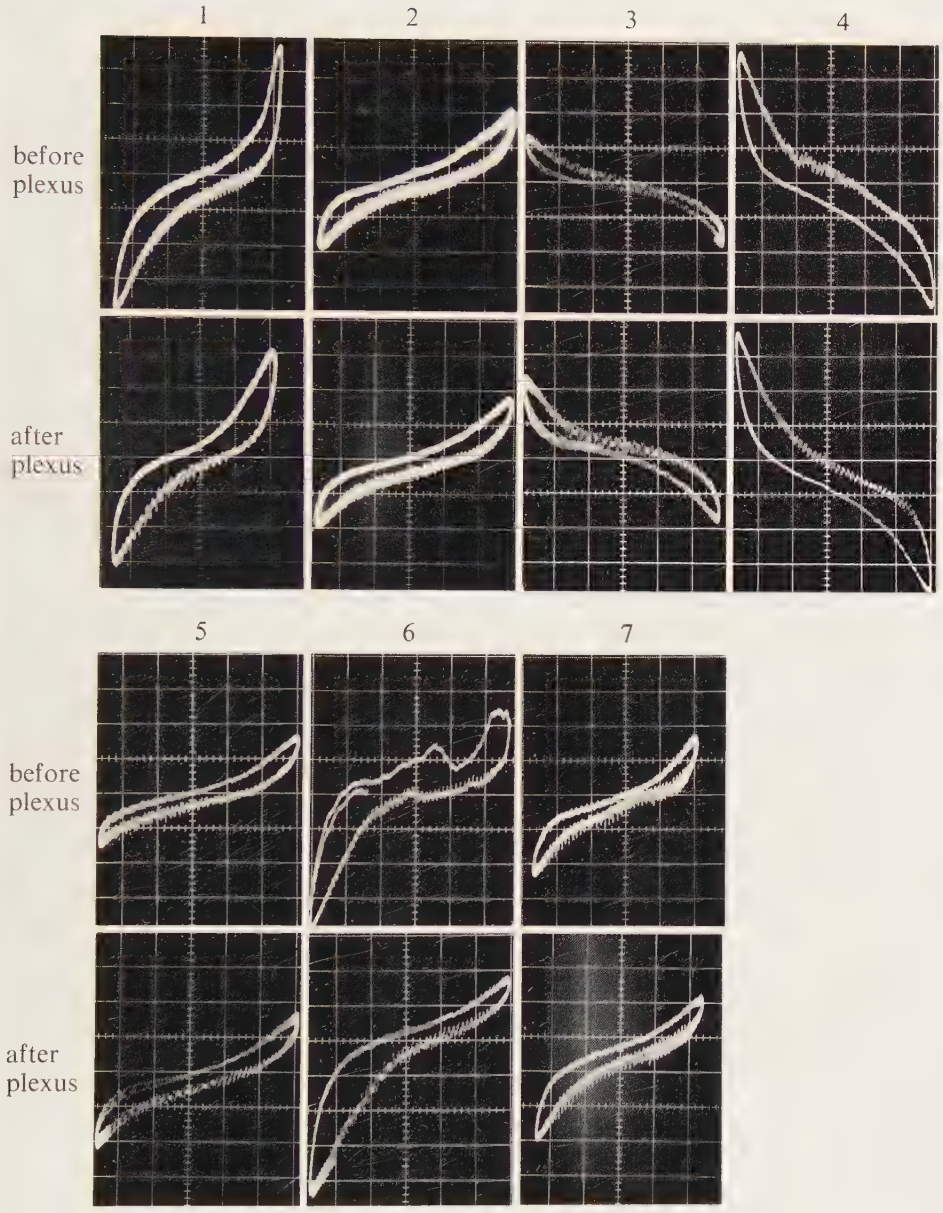


Fig. 38. Stiffness registrations before (*above*) and after (*below*) local axillary block anaesthesia. No major change in joint stiffness was found following anaesthesia indicating that no further relaxation was obtained through nerve block. Only in Case 1 was a slight decrease in stiffness noted. Case 6 showed pain-induced distorsions in the slope that disappeared following anaesthesia, while peak-to-peak torque remained unchanged.

at pH 4.4 according to Sundblad & Wallin-Nilsson (1962) and by the method according to Laurell (1966) using electrophoresis in agarose gel containing antibodies. *The α_2-globulin content* was measured using ordinary paper electrophoresis.[1]

Gripping strength was determined using the spygmomanometer method according to Davis (1958). The mean of three readings was taken.

Hand volume was measured according to the method by Smyth, Velayos & Hlad (1963) using water displacement and avoiding possible variation in wrist swelling. The mean of three readings was taken. The coefficient of variation was 1.34 per cent of the mean value derived from twenty consecutive readings on a normal subject during a period of two hours in the middle of the day.

Statistical methods

When the question was to what degree there existed an agreement in the changes for two variables, the phi-coefficient (Baggaley, 1964) was calculated. The corresponding significance test utilizes the relationship $\chi^2 \quad n \cdot (\text{phi})^2$ where n is the number of joint observations and χ^2 follows the χ^2 distribution with 1 degree of freedom.

When the main concern was to determine the degree of linear relationship between two variables the r-coefficient was calculated. Where a bivariate normal distribution could be assumed, the hypothesis of zero-correlation has been tested in a test of significance. The appropriate test is based upon the Student's t-distribution and is written $t = r \cdot \sqrt{(n-2)}/\sqrt{(1-r^2)}$, where n is the number of joint observations and t has $(n-2)$ degrees of freedom.

For the purpose of testing equality of two population means the usual t-test for this situation was applied.

Clinical application

Stiffness registrations were in most cases made bilaterally with the patient sitting relaxed in front of the apparatus with his arm on the arm rest and with the index finger connected to the finger holder. When the axis of rotation of the joint and the apparatus had been aligned the motor was started with a rotational velocity of 0.33 c/s. In very stiff joints the rotational displacement sometimes had to be reduced. During the first cycles it may happen that the patient is not sufficiently relaxed and produces distorsions in the slopes through voluntary muscle contractions resisting the motion. After a few cycles, however, most patients relax if pain on motion is not present, and smooth tracings are obtained.

[1] The orosomucoid and the ordinary paper electrophoretic determinations were kindly performed by Doc. L. Sundblad and Nurse Märta Wallin-Nilsson, Central Clinical Laboratory, Södersjukhuset, Stockholm.

CLINICAL MATERIAL

The clinical material consists of 45 patients treated at Sätra Hälsobrunn during the summer of 1965 and 1966, 17 patients being treated at the Department of Internal Medicine, Akademiska sjukhuset, Uppsala, 1965 and 1966, and 38 patients treated at the Department of Rheumatology, Regionsjukhuset, Örebro, from September, 1967, until April, 1969. The subjects were selected from patients with signs of digital RA but without severe deformities such as ulnar deviation or volar subluxation, mainly Steinbrocker stages and I and II, some, however, in stages III and IV without severe digital involvement.

Subjects

"Classical" RA[1]: 47 patients, 34 females and 13 males. Rheumatoid progression according to Steinbrocker et al. (1949): 1 patient was in stage I, 28 in stage II, 12 in stage III and 6 in stage IV.

"Definite" RA: 53 patients, 33 females and 20 males. 31 patients were in stage I, 19 in stage II, 3 in stage III, and none in stage IV.

The mean age in the female group was 55.3 years, in the male group 56.7 years. The duration of the disease defined as the period of continuous joint symptoms ranged from 1 to 40 years. The average duration was 13.2 years for classical females, 10.1 years for "definite" females, 9.6 years for "classical" males and 8.0 years for "definite" males. Table 8 shows some clinical and laboratory data of the one hundred patients with RA. Besides the RA cases, 10 healthy subjects were studied.

Treatment

All patients underwent conventional antirheumatic medication and physical therapy including systemic and local heat, assistive as well as active muscle exercises and progressive resistance exercises. Many patients also had occupational therapy.

Methods of clinical and laboratory examination

Each patient was examined by the author according to the methods outlined in Chapter 1. The 45 patients at Sätra Hälsobrunn were not examined with X-rays but as a rule this had been done earlier. No test for rheumatoid factor and no paper electrophoresis on serum was made in these patients and they therefore could only be classified as "definite" RA in 27 cases although some of them might well have been "classical" cases.

RESULTS

Stiffness in normal joints, arthritic joints and temperature influence upon stiffness in arthritic joints. These problems were studied at Sätra Hälsobrunn and the

[1] According to the American Rheumatism Association criteria (1958).

Table 8. *Clinical and laboratory data on 100 patients with RA*

Classification ...	"Classical" RA	"Definite" RA	"Classical" RA/ "Definite" RA
Number of cases	47	53	
Females	34	33	
Males	13	20	
Average age (years)			
Females			55.3
Males			56.7
Average duration of arthritis (years)			
Females	13.2	10.1	
Males	9.6	8.0	
Stage			
I	1	31	
II	28	19	
III	12	3	
IV	6	0	
Pos SSCA	28	17	

results were reported earlier (Bäcklund & Tiselius, 1967). *To summarize*, peak torques in ten healthy male and female students showed a mean value for males of 1.61 N and for females 1.00 N. Peak torques in five patients with RA showed a mean value of 2.64 N. There was considerable variation in stiffness among the patients depending on the degree of digital involvement and values ranging from quite normal to about 7.5–8 N were observed. No relation between stiffness values and ESR values appeared to exist. The results of Wright & Johns (1961) concerning the effect of cold and heat upon stiffness in healthy subjects could also be demonstrated in two patients with RA. Stiffness decreased slightly on heating and increased markedly on cooling.

Morning stiffness. As was shown by Bäcklund & Tiselius (1967), morning stiffness could be demonstrated using objective joint stiffness determinations. Three patients with active RA were measured throughout the day and a marked difference could be demonstrated between morning and afternoon values indicating the presence of morning stiffness. Although morning values in normal subjects could be of about the same magnitude as was found in arthritic subjects the normal joints did not show any variation in stiffness during the day indicating that morning stiffness and its decline during the day is a specific finding in active RA cases.

The question then arose whether the difference between morning and afternoon values was related to the degree of systemic disease activity. Nineteen patients were therefore measured between 7 and 8 a.m. and between 4 and 5 p.m. and each difference was plotted against the ESR. A correlation coefficient

of r 0.60 in the relation between the differences in morning–afternoon stiffness values and the ESR was found. If cases with an ESR exceeding 45 mm/hour were compared with those showing lower values a significant difference (t 3.80, P 0.001) was found between the means in differences of the two groups.

To summarize, active cases of digital RA showed morning stiffness that correlated with the systemic disease activity (ESR), r 0.60. Cases with higher disease activity (ESR $\geq$ 45 mm/hour) showed more pronounced morning stiffness values (t 3.80, P 0.001). No morning stiffness could be demonstrated in normal subjects.

Stiffness in relation to hand volume and gripping strength. Simultaneous registrations of stiffness in the second MP joint, hand volume and gripping strength were made between 7 and 8 a.m. and between 4 and 5 p.m. The following relation between these variables was obtained. *Stiffness–hand volume.* An almost linear positive correlation (r 0.91) was found when measuring both hands in seven patients with digital RA. A decreasing hand volume is apparently parallel to a decreasing elastic stiffness in the MP joints. No major change in viscous stiffness was observed. *Stiffness–gripping strength.* There was a weak negative correlation (r 0.24) between elastic stiffness and gripping strength but the results do not allow definite conclusions concerning this relation. *Hand volume–gripping strength.* No correlation (r 0.13) could be demonstrated between hand volume and gripping strength in this study.

To summarize, a strong positive correlation ($r = 0.91$) was found between elastic stiffness at the second MP joint and hand volume when comparing morning and afternoon values. No change in viscous stiffness was noted. No definite relation between elastic stiffness and gripping strength or between hand volume and gripping strength could be demonstrated in this study.

Stiffness in relation to systemic disease activity. As there exists such a considerable variation in the elastic stiffness in MP joints in cases with digital RA and as apparently no relation is found between stiffness intensity values and systemic disease activity, it would seem more interesting to investigate whether *changes* in stiffness from one time to another bore any relation to *changes* in systemic disease activity. Sixteen patients were followed with simultaneous registration of elastic stiffness in their second MP joints and systemic disease activity with intervals of about two months. No correlation could be demonstrated between changes in stiffness and changes in ESR (r 0.01). Correlation coefficients in the relation between stiffness and orosomucoid content in serum were r 0.15 for orosomucoid determined by acid paper electrophoresis and r 0.28 for orosomucoid determined by agarose gel electrophoresis. The relation between changes in stiffness and changes in α_2-globulin levels according to ordinary paper electrophoresis was r 0.30. None of

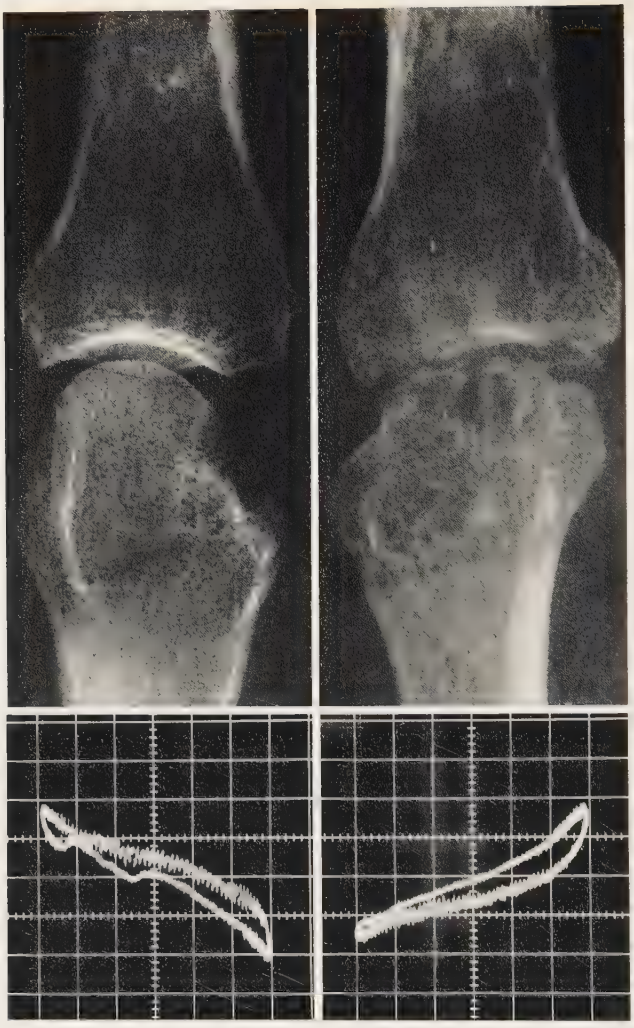


Fig. 39. Left and right second MP joint with corresponding stiffness slopes from a patient with RA. In spite of marked radiologic changes with cartilage destruction and joint space narrowing in the right joint as compared with only moderate changes in the left, a stiffer slope was found in the latter measuring 3.92 N versus 3.43 N on the opposite side. Radiologic changes appear to play no major role among factors contributing to joint stiffness.

the above mentioned correlation coefficients was significant. Correlation coefficients between the different measures of systemic disease activity were as follows: r (ESR; orosomucoid at 4.4) 0.52 (P 0.05), r (ESR; orosomucoid in agarose gel) 0.54 (P 0.01), r (ESR; α_2- globulin) 0.34, r (orosomucoid at pH 4.4; orosomucoid in agarose gel) 0.82 (P 0.001), r (orosomucoid at pH 4.4; α_2-globulin) 0.50 (P 0.05), r (orosomucoid in agarose gel; α_2- globulin) 0.65 ($P < 0.001$).

To summarize, no evidence has been found that elastic stiffness in MP joints in patients with digital RA is correlated with the degree of systemic disease activity or to changes in it from one time to another.

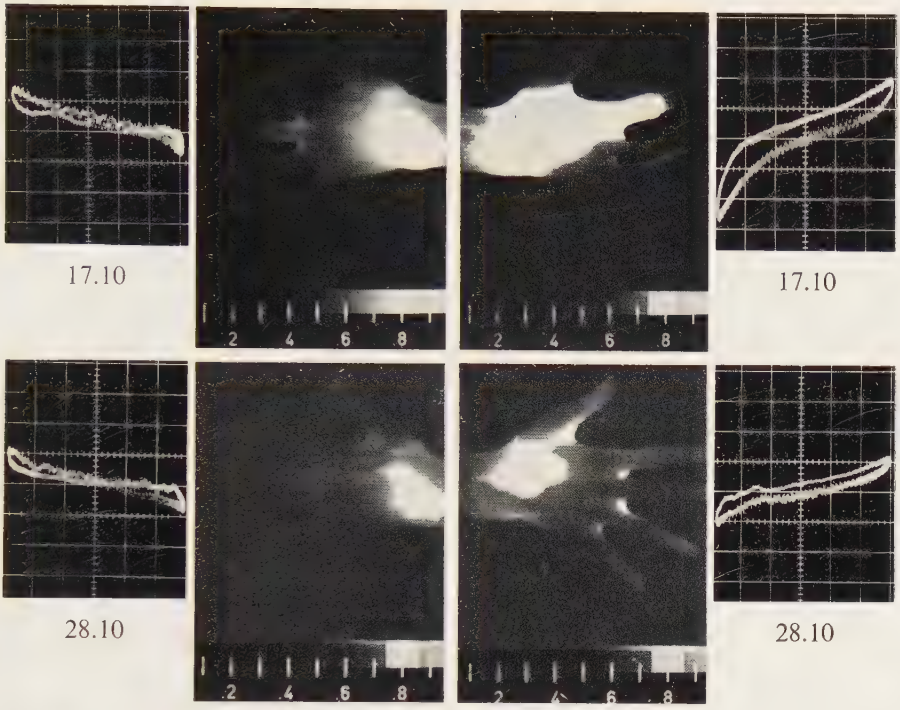


Fig. 40. Inflammatory changes with soft tissue swelling and increased heat emission give rise to a marked increase in elastic as well as viscous stiffness as this case of RA shows. On admission the right second MP joint and surrounding tissues showed active inflammation according to the clinical and thermographic findings while the left wrist showed synovitis around the caput ulnae. Eleven days of antirheumatic treatment (repeated local steroid infiltrations) revealed decreasing heat emission primarily at the right second MP joint but also a slight decrease around the left caput ulnae was noted. Peak torque at the second right MP joint fell from 4.60 N to 2.35 N and the planimetric area fell from 4.20 Ncm/c to 2.20 Ncm/c. No major change in stiffness in the left second MP joint was found.

Stiffness in relation to rheumatoid changes in the joint. Stiffness in relation to the local disease process in the joint was investigated with regard to radiologic changes and local inflammatory activity by means of infrared thermography. *Radiologic changes.* Fig. 39 illustrates the relation between stiffness and radiologic changes in the second MP joints in a patient with RA. In spite of marked radiologic changes in the right joint, stiffness registration revealed a somewhat lesser elastic stiffness in this joint as compared with the left MP joint where only moderate radiologic changes were present. This disproportion between stiffness and radiologic changes was observed in several MP joints indicating that cartilage destruction and joint space narrowing apparently do not contribute significantly to elastic stiffness. *Local joint inflammatory changes.* Fig. 40 illustrates a typical case of digital RA with thermographic

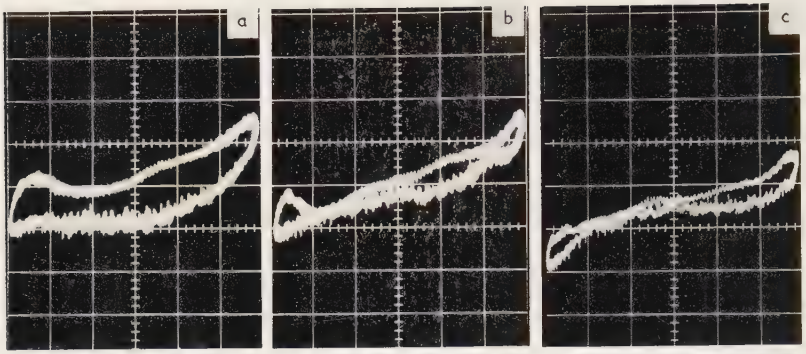


Fig. 41. Tenosynovitis in the flexor tendon of the right second MP joint in a patient with RA giving rise to a "trigger finger" phenomenon in the slope. (*a*) Before local infiltration of steroid with markedly increased planimetric area and a distorsion in the slope at the beginning of flexion. (*b*) Six days and (*c*) twelve days following repeated infiltrations producing marked decrease in viscous stiffness and disappearence of the distorsion. Elastic stiffness remained unchanged.

signs of active synovitis in the right second MP joint accompanied by a marked increase in elastic as well as viscous stiffness. After local steroid infiltrations, both temperature elevation and stiffness decreased. This phenomenon has been observed in several other cases of active digital RA and among therapeutic effects after synovectomy of the joint, decreased elastic stiffness has been observed earlier (Bäcklund & Tiselius, 1967). The difference in elastic stiffness in two MP joints with normal radiologic findings three years after unilateral synovectomy was 1.18 N (3.23 N in the synovectomized joint as compared to 4.41 N in the nonsynovectomized joint). The inflamed joint capsule apparently contributes to a considerable degree to elastic stiffness.

To summarize, cartilage destruction and joint space narrowing appear to play only a minor role among the different factors acting upon the joint contributing to stiffness, whereas inflammatory changes in the joint capsule as seen by temperature elevation and swelling and removed by synovectomy apparently constitute important contributors to joint stiffness.

Stiffness in relation to rheumatoid changes in flexor and extensor tendons. Flexor tendons. Local tenosynovitis in the flexor tendons of the index finger may give rise to distorsions in the stiffness slope and increased viscous stiffness as is illustrated in Fig. 41. *Extensor tendons.* The extensor tendon sheaths over the dorsum of the wrist may also become involved in a rheumatoid tenosynovitis. The fourth tendon tunnel contains the common extensors and the extensor indicis proprius. If synovial thickening and proliferation infiltrate the tendons at this region this may add to increased viscous stiffness at the second MP joint whereas elastic stiffness is not influenced to any major degree. Table 9 illustrates peak torques and planimetric areas of slopes registered from MP joints

Table 9. *Peak torques (N) and planimetric areas (Ncm/c) in two patients with RA showing marked dorsal tenosynovitis at the wrist, one bilaterally.*

Local steroid infiltrations were given after the first (I) and second (II) joint stiffness registration. Decreasing, primarily viscous, stiffness was observed during the follow-up period.

Pat.	I	Interval (days)	II	Interval (days)	III
V. S.					
Right wrist					
peak torque	3.93	7	3.04	30	3.04
planimetric area	5.64		1.41		1.67
Left wrist					
peak torque	4.02	7	2.84	30	3.24
planimetric area	2.46		1.53		1.08
E. B.					
Right wrist					
peak torque	5.20	3	4.50	53	3.82
planimetric area	7.75		5.88		3.11

in two patients with RA showing marked dorsal tenosynovitis at the wrist treated with local steroid infiltration.

To summarize, rheumatoid changes in flexor and extensor tendons produce increased viscous stiffness and distorsions in the stiffness slopes whereas elastic stiffness remains proportionately unchanged.

COMMENTS

The results of this study are in agreement with the findings by Wright & Johns (1960*a*, 1960*b*, 1961) who studied joint stiffness in normal subjects as well as in arthritic subjects. Some additional comments must, however, be given concerning joint stiffness in patients with RA.

As there exists considerable individual variations in stiffness among the patients depending on the degree of local digital involvement rather than on the degree of systemic disease activity, it would not seem meaningful to compare absolute stiffness values in different patients with simultaneously obtained ESR values. Morning stiffness determinations appear to be of greater interest in this respect. It was shown in this study that the values for morning stiffness were higher in patients with a more active disease as expressed in the ESR. Only a weak negative correlation between stiffness and gripping strength could be demonstrated whereas stiffness and hand volume showed a strong positive correlation. Wright & Plunkett (1966) found a diminished diurnal variation in gripping strength with increased absolute values in a patient with RA treated with ACTH. This phenomenon was accompanied by a decrease in subjective morning stiff-

ness, whether in intensity or duration is, however, not stated. A morning increase in hand volume was found in normal as well as in arthritic subjects by Scott (1960). This finding was probably largely attributable to the local factor of immobility during sleep and to the diminished venous return due to lack in muscular pumping action. Patients with a less active disease may move their extremities with greater ease offering a more effective venous return from distal parts giving rise to a more rapid decrease in hand volume values in the early morning when limbering up. When hand volume decreases elastic stiffness also decreases and morning stiffness, i.e., the difference between morning and afternoon values, declines. It thus seems as if improved muscle function in the less active diseased state via improved muscular pumping with more rapid venous return in the upper extremity helps to relieve morning stiffness. This could also explain the weak negative correlation between simultaneously determined gripping strength and elastic stiffness observed in this study. The improvement in gripping strength precedes the decrease in stiffness which is secondary to the increased muscle strength producing diminished hand volume. The same explanation can be given for the lack of correlation between gripping strength and hand volume, the latter is secondarily influenced by the former.

No correlation was found between changes in elastic stiffness and changes in systemic disease activity on repeated examination at two-month intervals. These examinations were made in the afternoon when morning stiffness had subsided in most patients. Afternoon stiffness values did not vary in proportion to systemic disease activity but it is possible that morning values would have shown greater variations from time to time beacuse, as was shown in this study, it is the *difference* between morning and afternoon values that is significantly correlated to systemic disease activity.

It may perhaps seem astonishing that radiologic changes with cartilage destruction and joint space narrowing play only a minor role among factors contributing to joint stiffness. The cause of stiffness, as was found also by Wright & Johns (1961) in their study of arthritic patients, is primarily due to changes in the joint capsule rather than to damaged joint surfaces. They showed that only in severely damaged joints with marked clinical and radiologic deterioration could friction be demonstrated while elastic and viscous stiffness apparently was not influenced. Local joint disease activity measured by means of infrared thermography is a major contributor to elastic as well as viscous stiffness and joint stiffness determinations constitute a method to study the effect of, for instance, synovectomy.

Tenosynovitis is an important factor causing primarily increased viscous stiffness at the joint. It is, however, natural to assume that effusion and synovial thickening in tendon sheaths give rise to increased viscous resistance against tendon motion. If the planimetric area of the slopes is magnified even at low

rotational velocities this implies significant viscous stiffness and this was often observed when the tendons were involved with tenosynovitis.

No contribution of reflex or active muscle contraction to the stiffness measured at the joint was found in this study using a rotational velocity of 0.33 c/s. This is in agreement with the findings of Wright & Johns (1960*a*, 1960*b*, 1961) and Long, Thomas & Crochetiere (1964). If contractions occurred, they were observed as distorsions in the tracing and often connected with pain on joint motion.

CONCLUSION

Further clinical experience of objective joint stiffness determinations in patients with digital RA has been collected. Evidence has been found that stiffness in rheumatoid MP joints is due primarily to local inflammatory changes in the joint capsule which give rise to increased elastic stiffness. Joint swelling and temperature elevation is accompanied by increased elastic and, to a certain degree, viscous stiffness. Radiologic changes in the joint apparently play no major role among the factors contributing to stiffness provided that ulnar deviation or volar subluxation is only mild and does not prevent joint motion to any considerable degree. Increased viscous stiffness is commonly observed in connection with tenosynovitis while elastic stiffness is not influenced to any considerable degree by tendon sheath involvement. Morning stiffness intensity expressed as the difference between morning and afternoon stiffness values was found to correlate positively with the degree of systemic disease activity and was interpreted as a secondary phenomenon due to increased joint swelling and hand volume in connection with partly impaired muscle function with insufficient muscle pumping action. Changes in afternoon stiffness values when morning stiffness had subsided were not correlated to changes in systemic disease activity. The method used for stiffness registrations undoubtedly suffers from certain disadvantages, the principal one being that estimations are confined to the second MP joints. These joints are, however, often involved in RA. The results obtained have shown that the method may be used in studying the influence of different clinical and laboratory findings upon digital joint stiffness in RA. If oral or parenteral administration of antirheumatic drugs are given, changes in morning stiffness may reflect decreased systemic disease activity. If local antirheumatic treatment is given (synovectomy, steroid infiltration) changes in elastic or viscous joint stiffness may occur. There is considerable room for more objective parameters in rheumatology and joint stiffness determinations may be used when studying a common complaint in rheumatic patients.

Chapter 4

DIFFERENCES BETWEEN MEASURED AND EXPERIENCED JOINT STIFFNESS

Owing to the conflicting results often obtained when comparing subjective complaints with objective clinical findings in RA, it was considered to be of interest to study possible differences between measured and experienced stiffness in the second MP joint in relation to intellectual properties and some personality factors within the rheumatic patient. Some patients have a tendency to exaggerate the description of their symptoms whereas others seem to be able to describe their symptoms in agreement with what can be observed during the clinical examination. Using stiffness registration and the patient's statement about the stiffness in his MP joints simultaneously, the following investigation concerning the relation between objective and subjective estimation of this disease manifestation in RA was performed.

MATERIAL

Forty-two patients with "classical" or "definite" RA according to the criteria proposed by the American Rheumatism Association (1958) belonging to the clinical material in Chapter 3 were studied. They all showed digital involvement and were suitable for joint stiffness determinations. Mean age was 54.8 years.

METHODS

Objective joint stiffness determination in the right second MP joint was made according to the technique described in Chapter 3.

Subjective joint stiffness estimation was registered with regard to (*a*) intensity (+ + + values exceeding 5.88 N, + values between 5.88 N and 3.92 N, 0 values below 3.92 N). This division of the different value limits was made according to empirically observed elastic stiffness values in the material. (*b*) Changes between three consecutive examinations. (*c*). Morning stiffness duration in minutes.

Gripping strength was determined according to the method described in Chapter 3 and used as an indirect measure of joint stiffness according to Wright

Table 10. *Results of objective elastic joint stiffness determinations in the second right MP joint (ponds), subjective joint stiffness intensity (implies values exceeding 600 ponds 5.88 N, · implies values between 600 ponds 5.88 N and 400 ponds 3.92 N, 0 implies values below 400 ponds 3.92 ponds), differences between afternoon (4 p.m.) and morning (9 a.m.), gripping strength values (mm Hg), subjective morning stiffness duration (minutes) and results of the SRB test (stanine values)[1] and the MPI test.*

Twenty-four patients took part in the comparison between differences in afternoon and morning gripping strength values and duration of morning stiffness. These patients generally got up round 7 a.m. One patient (no. 3) did not take part in objective joint stiffness determinations and two patients (nos. 4 and 5) did not take part in the SRB test.

Patient no.	SRB stanine value	MPI			Elastic stiffness			Subjective stiffness			Difference gripping strength afternoon–morning			Duration subjective morning stiffness		
		E	N	L	I	II	III	I	II	III	I	II	III	I	II	III
1	5	15	44	9	520	600	300	+++	+	+	35	40	38	60	45	60
2	6	33	2	6	560	500	500	+	+	+	0	−2	0	60	30	30
3	7	21	0	11	—	—	—	—	—	—	15	3	3	120	60	60
4	—	16	5	15	300	480	380	+	0	0	18	9	16	270	0	0
5	—	32	34	15	300	280	240	+++	+++	+++	0	10	0	360	360	360
6	6	31	15	12	560	740	600	+	+	+	5	2	0	10	60	60
7	6	12	33	3	260	480	460	+++	+	+	0	4	4	360	60	30
8	6	16	22	12	650	480	520	+	0	+	4	4	4	30	0	10
9	6	16	46	4	400	380	360	+++	+	+++	5	10	15	420	90	360
10	1	30	11	12	540	480	400	+	+	+	0	3	5	60	60	60
11	5	19	16	9	650	540	500	+++	+	+	0	2	2	210	210	210
12	8	22	41	5	280	300	280	+	+++	0	−25	−18	−10	30	30	0
13	5	24	20	10	460	540	540	+	+	+++	25	8	5	60	180	180
14	6	20	17	8	520	400	520	+++	+	+++	25	25	28	180	150	180
15	5	24	14	10	500	400	260	+++	+++	+	20	12	0	180	150	120
16	6	31	10	11	250	340	280	+	+++	+						
17	6	13	27	8	480	420	460	+	+++	0						
18	7	20	10	7	340	560	690	+	+++	+++						
19	7	28	6	9	200	220	230	+	+	+						
20	6	28	26	6	500	470	550	+	+++	+						
21	3	21	10	12	430	260	300	+	+	+						
22	3	13	4	12	630	670	500	+++	+++	+						
23	4	31	29	6	260	340	280	+	+	+++						
24	3	16	10	9	400	420	400	+	+	+						
25	9	41	12	11	400	560	380	+	+++	+						
26	6	24	32	12	480	680	480	+++	+	+						
27	7	23	10	11	820	800	860	+++	+++	+++						
28	4	28	5	14	360	400	510	+	+	+++						
29	8	33	10	7	780	780	720	+	+	+	5	5	5	30	20	10
30	5	28	6	12	560	780	560	+	+	+++	27	30	40	120	120	150
31	7	28	8	6	540	320	260	+++	+	+	32	5	10	180	60	60
32	3	38	4	10	560	860	420	+++	+++	+	25	20	25	180	210	180
33	5	27	3	5	630	630	540	+++	+++	+++						
34	7	14	22	8	300	600	540	+++	+	+	5	8	5	210	180	180
35	7	37	7	10	650	670	670	+	+	+	6	0	−10	60	60	60
36	7	28	11	3	660	660	500	+	+	+	2	0	3	30	30	30
37	6	29	31	7	760	560	680	+	+	+++	−5	2	5	90	60	30
38	4	30	12	11	1820	1040	1200	+++	+	+	0	5	−5	15	10	10
39	8	38	20	9	340	340	320	+++	+++	+						
40	6	28	19	5	600	380	510	+++	+	+++						
41	3	17	26	6	370	470	380	+++	+	+						
42	3	16	7	7	540	600	760	+	+	+						

[1] Refers to "standard nine" values.

Table 11. *Psychometric data in patients with varying degrees of agreement between objective and subjective joint stiffness intensity.*

Agreement could be present between none to three times on consecutive measurements.

Agreement subjective-objective estimations (times)	SRB mean values	E mean values	N mean values	L mean values	*n*
3	4.17	22.33	8.83	9.83	6
2	5.00	25.63	17.37	7.50	8
1	5.31 ($n=16$)	22.59	19.94	9.48	17
0	6.78 ($n=9$)	29.50	16.60	8.40	10

(1959) and Scott (1960). Differences $\geqslant 15$ mm Hg were required to indicate a real change in the strength values.

Psychological evaluation included the SRB test for intellectual capacity according to Dureman & Sälde (1959)[1] and the MPI test for neuroticism and introversion assessment according to Eysenck (1959). The limits for these variables proposed by Åström & Ölander (1960) were used (scores > 17.90 imply neurotic personality, scores < 26.43 imply introvert personality).

RESULTS

Table 10 shows the results of objective elastic stiffness determinations, subjective stiffness intensity, duration of subjective morning stiffness and differences

Table 12. *Psychometric data in patients with varying degrees of agreement between unidirectional changes in objective and subjective joint stiffness.*

Agreement could be present in between none to two paired comparisons at consecutive measurements.

Agreement subjective-objective estimations (times)	SRB mean values	E mean values	N mean values	L mean values	*n*
2	7.00	28.00	20.14	8.71	7
1	5.53	26.87	12.20	8.07	15
0	5.00 ($n=17$)	22.00	18.65	9.65	19

[1] Kindly performed by Miss Maiken Elfström, B.A. and Mrs. Margareta Hedén-Chami B.A.

Table 13. *Psychometric data in patients belonging to alternatives A-B and C-D, respectively (for explanation, see Fig. 42), in the comparison between differences in afternoon and morning gripping strength values and the subjectively experienced duration of morning stiffness.*

Patients belonging to alternative	SRB mean values	E mean values	N mean values	L mean values	*n*
A–B	5.90 ($n=17$)	24.78	15.39	8.70	18
C–D	5.50 ($n=5$)	19.60	25.40	9.30	6

between morning and afternoon gripping strength values measured at about 9 a.m. and 4 p.m. respectively. Morning stiffness duration in minutes was inquired about at the examination at 4 p.m. The results of the SRB and MPI tests are also given.

The relation between elastic and experienced joint stiffness intensity on three consecutive occasions is illustrated in Table 11.

The relation between unidirectional changes in elastic stiffness and experienced stiffness intensity on three consecutive occasions is illustrated in Table 12.

The relation between the subjectively experienced duration of morning stiffness and gripping strength is illustrated in Table 13.

COMMENTS

If a subjective description of joint stiffness is used as a diagnostic criterion (American Rheumatism Association, 1958) or as a disease activity parameter in RA (Lansbury, 1958) or in epidemiological studies in RA (Cobb, Warren, Thompson & Ciocco, 1954), this study seems to indicate that personality factors might influence the accuracy of the evaluations. It has been possible to check the relation between objective and subjective joint stiffness with regard to intensity and unidirectional changes. Indirect measurements of joint stiffness, viz., gripping strength according to Wright (1959) and Scott (1960), have been compared with the patient's interpretation of joint stiffness duration. Wright pointed out that the arthritic patient experiences stiffness in the fingers when strength of grip falls below a critical level. Strength of grip could thus constitute an indirect way of measuring joint stiffness in the hand. Scott demonstrated the subjective complaint of morning stiffness in patients with RA by a matutinal increase in objective joint stiffness and hand volume and a decrease in gripping strength. The following schematic drawing may be used as an illustration of this

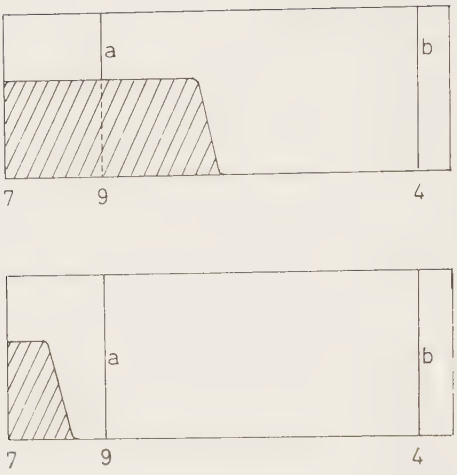


Fig. 42. Schematic drawing of the hypothetical relation between subjective morning stiffness and gripping strength according to Wright (1959) and Scott (1960). Morning stiffness = lined area, a = gripping strength at 9 a.m. and b = gripping strength at 4 p.m. Alternatives *in agreement* with the theory of Wright and Scott imply $a < b$ when stiffness duration ≥ 120 minutes (alternative A) or $a = b$ when stiffness duration < 120 minutes (alternative B). Alternatives *not in agreement* with the theory imply $a < b$ when stiffness duration < 120 minutes (alternative C) or $a = b$ when stiffness duration $\geq$ 120 minutes (alternative D).

theory (Fig. 42). This assumption has been used in the present study when comparing subjective morning stiffness duration and gripping strength.

The following observations have been made and might be worth remembering when using subjective joint stiffness as a parameter in the evaluation of patients with RA.

1. Ability to describe stiffness intensity in agreement with objective stiffness was lower in those patients that scored higher neuroticism values.
2. Ability to describe unidirectional changes in stiffness over periods of time in agreement with objective stiffness values was lower in those patients that scored lower IQ levels.
3. Ability to describe morning stiffness duration in agreement with gripping strength values (as indirect measures of stiffness in the hand) was lower in those patients that scored higher neuroticism values.

Not only in Lansbury's Systemic Index (Lansbury, 1958) but also in numerous other methods for clinical evaluation of systemic disease activity in RA (see Table 1), subjectively estimated joint stiffness is used as a parameter together with other subjective items such as fatigue, loss of apetite, sense of well-being, etc. It seems apparent that the patient's interpretation of such parameters could also be influenced by psychological factors and should therefore be looked upon with caution.

Chapter 5

STUDIES ON MUSCLE WEAKNESS IN RHEUMATOID ARTHRITIS

Very often patients with RA complain of muscle weakness, especially in manual gripping, and this appears to be such a common symptom that gripping strength has become a parameter of systemic disease activity in widespread use not only in connection with antirheumatic drug trials (Cohen & Calkins, 1958; Vaughn, Howell & Keim, 1959) but also in studying spontaneous fluctuations in disease activity (Lansbury, 1958). One method has almost entirely been used in this context, viz., the sphygmomanometer method according to Davis (1958). In this method the patient's ability to compress an inflated cuff under standardized conditions is registered. A mean of three readings is used and Lansbury (1966) claims that even small changes in systemic rheumatoid activity are registered by this technique provided deformities, muscle fibrosis and atrophy are not sufficient to interfere. Gripping strength is considerably affected by joint pain not only in the hand but also in the elbow and shoulder and it appears that the soft sphygmomanometer cuff is comfortable for the painful hand as compared with, for instance, Collin's dynamometer (as quoted by Zoth, 1936) which is in common use today. There is general agreement that the sphygmomanometer method is a reliable method of measuring gripping strength in patients with RA (Lansbury, 1966).

If muscle weakness is such a common finding and also used as a disease activity parameter in RA it is surprising that so little has been done in attempts to perform systematic and more extended assessments during the clinical course of the disease. Although it must be remembered that muscle testing constitutes a semi-objective method depending on the motivation of the patient, more information appears to be needed concerning variations in strength and its relation to other disease manifestations reflecting systemic as well as local activity in RA. Especially studies of muscle contractions not restricted by pain should be of interest in this respect. Apparently other factors besides pain might influence muscle strength, e.g., myositis, neuropathia, peripheral nerve compression, tendon ruptures and joint effusion. Some of these factors are reversible and subject to variations related to the local joint disease process. Moritz (1963) reported findings indicating a relation between electro-

myographic changes in the muscle and the activity of the local arthritic process in certain adjacent joints. Considerable improvement in muscle function paralleled by an increase in the mean potential duration in connection with steroid treatment of cases of polymyositis associated with RA was found by Pitkeathly & Coomes (1966). de Andrade, Grant & Dixon (1965) reported on joint distension and reflex muscle inhibition in the knee in patients with RA.

That so little has been done in muscle strength assessments in RA might also be due to a lack in measuring devices. Tornvall (1963) and Mannerfelt (1966) have given comprehensive surveys of earlier work in this field. Muscle strength can be measured either isotonically or isometrically. In isotonic determination it is the work capacity rather than the muscle strength that is measured and standardizing is difficult. This method might be tiring for the test object and also pressure-induced variations in joint friction and joint pain during motion might occur. There is a close correlation between maximal isometric and isotonic muscle strength (Asmussen, Hansen & Lammert 1965) and most investigators have used isometric testing technique. Important refinements in the isometric muscle test technique have been made by Asmussen, Heebøll-Nielsen & Molbech (1959), Tornvall (1963) and Bäcklund & Nordgren (1968). These authors have developed methods that allow isometric testing under standardized conditions, which has greatly stimulated the interest in performing tests on muscle weakness in clinical practice.

The purpose of the present work has been to study some clinical problems concerning muscle weakness in patients with RA. Isometric testing has been used and as far as possible only painless muscle contractions have been utilized in order to eliminate pain as a major inhibiting factor and to focus interest on the relation between strength values and other possible restricting factors.

The following main questions have been studied:

1. Degree of muscle weakness in patients with RA as compared with normal subjects.
2. Relation between muscle strength values recorded in the extremities (expressed as a total muscle index) and ESR.
3. Relation between changes in muscle strength values recorded in the extremities (expressed as an abbreviated muscle index) and changes in systemic disease activity over prolonged periods of time.
4. Effect of physical therapy upon isometric muscle strength.

METHODS

The method for measuring the maximum isometric muscle strength described by Asmussen, Heebøll-Nielsen & Molbech (1959) including the Darcus dyna-

mometer (Darcus, 1953) and Asmussen & Heeboll-Nielsen (1961) was used with some modifications.

The dynamometers were based on the strain-gauge principle. An amplifier (KWS/T-5) and a coupling unit (UD6 II-5: Hottinger Messtechnik, Darmstadt, Germany) were used both to supply current to the bridges and for amplification of the output signals. These signals were recorded with a potentiometer recorder (H. pot. recorder, Control Instruments Ltd., Birkenhead, England).

The maximal voluntary isometric muscle strength in different muscle groups was measured during practically isometric contractions. The subject investigated was asked to attempt certain movements in standardized positions and to strive to avoid jerks. When the maximal level of contraction was reached it had to be held for about three seconds. Each test was preceded by thorough instructions and a demonstration of the attempted movement wanted. The highest value of three attempted movements was used as an expression of the maximum isometric muscle strength. In arthritic patients this value very often was reached during the first attempt. Occasionally more than three attempted movements were required to determine the maximum strength value, viz., when the test values showed a steady increase during the first three attempts. The interval between each attempt was about 15–20 seconds.

Description of the muscle test

The method according to Asmussen et al. (1959) was modified to fit arthritic patients. Extension and flexion of the trunk and test of hip muscles was not used because these movements necessitate a standing subject. The arthritic patient may have difficulties in standing upright on one foot while attempting to perform prescribed movements due to pain in his knees or ankles. In addition, trunk muscles reflecting spine involvement and hip muscles reflecting hip involvement can be considered of limited interest in patients with RA in whom these joints are proportionately seldom affected. Flexion and extension of the elbows was included in the modified muscle test.

The following twelve tests were made bilaterally when calculating the total muscle index (see below).

Tests for upper extremities

Gripping strength: The patient was tested sitting on a chair. The handle setting of the dynamometer was adjusted to fit the size of the subject's hand and noted beacuse this setting had to be used during repeated testing. One handle rod was held in the palm and one at the middle phalanges. The elbow was flexed 90°.

Participating muscles: m.m. flexor digitorum superficialis et profundus, m.m. flexor pollicis longus et brevis, m. opponens pollicis, m. adductor pollicis, m.m. interossei, m.m. lumbricales.

Pinching: The patient sitting with the tip of the thumb pressed against the tip of the index finger with the dynamometer in between.

Participating muscles: m.m. flexor pollicis longus et brevis, m. adductor pollicis, m. opponens pollicis, m. interosseus dorsalis I, m.m. flexor digitorum superficialis et profundus of second finger.

Pronation handle: The patient sitting with the lower arm held between pro- and supination and the elbow at side flexed 90°.

Participating muscles: the same as for gripping stength, m. pronator teres, m. pronator quadratus, m. flexor carpi radialis.

Supination handle: The patient in same position as when testing with pronation handle.

Participating muscles: the same as for gripping strength, m. biceps brachii, m. brachialis, m. brachio radialis.

Elbow extension: The patient was examined sitting on a chair with the upper arm vertical and the elbow flexed 90 . The arm was held between pro- and supination. The fastening strap of the dynamometer was placed at the level of the styloid process of the ulna.

Participating muscles: m. triceps brachii.

Elbow flexion: The same position as for elbow extension but with the fastening strap at the level of the styloid process of the radius.

Participating muscles: m. biceps brachii, m. brachioradialis, m. brachialis.

Horizontal pull: The patient grasps a sword-like handle at shoulder height sitting erect with elbow flexed 90 . The back is against the wall with a strap tightened around the chest under the arms.

Participating muscles: the same as for gripping strength, m. brachioradialis, m. biceps brachii, m. latissimus dorsi, lower part of m. trapezius.

Horizontal push: The patient in the same position as for horizontal pull.

Participating muscles: M. triceps brachii, m. serratus lateralis, upper part of m. trapezius.

Tests for lower extremities

Knee extension: The patient in sitting poisiton with hip and knee in 90 flexion with the foot resting on a plate. Fixation with straps at the ankle and immediately below the knee. In addition, the patient contributed to fixation of the trunk by holding onto the chair with one hand and to the vertical steel post to which the Darcus dynomometer is mounted with the other hand.

Participating muscles: M. quadriceps femoris.

Knee flexion: The patient in same position as for knee extension. Staps at the ankle and in front of the flexed knee.

Participating muscles: M. biceps femoris, m. semitendineus, m. semimembranaceus, m. gracilis, m. sartorius.

Plantar flexion ankle: The patient in sitting position as when measuring attempted knee movements. The foot was placed on the dynamometer plate and fixed with one strap around the wrist and one at the metatarsophalangeal joint level.

Participating muscles: M. gastrocnemius, m. soleus.

Dorsal flexion ankle: The patient in the same position as for plantar flexion ankle but with loosened ankle strap to avoid influence upon the action of the dorsal flexors.

Participating muscles: M. tibialis anterior, m. extensor hallucis longus, m. extensor digitorum longus, m. fibularis tertius.

The values for the maximal isometric muscle strength determinations were given in kiloponds (kp) with the exception for tests with pronation and supination handle in which kilopond centimeters (kpcm) were used. Estimation of the lever was of importance in attempted movements at the elbow, the knee and the ankle. These levers were measured in cm for each patient and were noted when studying the patient in follow-up tests.

Regular complete calibration of the strain gauges using known weights was performed. For every strain gauge the whole measuring range was checked. The calibration values showed a linear relation to successively increasing loads with only minor variation.

The sequence of testing the different muscle groups was the same during repeated tests beginning with the upper extremities, right side.

Normal values for maximal isometric muscle strength

Asmussen & Heebøll-Nielsen (1961), Tornvall (1963) and Bäcklund & Nordgren (1968) have published normal values for maximal isometric muscle strength in healthy subjects. In the present investigation the technique according to Asmussen et al. (1959) has been utilized; therefore it was suitable to use the normal values for adult men and women reported by Asmussen & Heebøll-Nielsen (1961). For elbow flexion and extension, however, no normal values were given in their report and because of these the normal values of Bäcklund & Nordgren (1968) for these tests have been used. A reduction for women was made in proportion to the relation between values for horizontal pull for men and women found in the report by Asmussen & Heebøll-Nielsen (1961). Although some doubt can be thrown upon wether the values for plantar flexion of ankle really constitute maximum values in the report of Asmussen & Heebøll-Nielsen they have been used anyhow.

Total muscle index

The present method for evaluation of isometric muscle strength was designed with the intention to use it in clinical rheumatological work to collect information about the general muscle status (for which the term muscularity has been used by Tornvall, 1963) of the patient with RA. The general as well as local degree of muscle weakness in the individual patient was considered of interest. In this context it appeared necessary to summarize the individual muscle test values in a total muscle index (TMI). Methods for summing up muscle test values for total muscularity estimations have been described earlier by Martin & Rich (1918), Bethe & Fischer (1929), Clarke (1954) and Lindegård (1956). These methods have been reviewed by Tornvall (1963). The TMI used in this investigation is obtained by adding the values of the individual tests expressed in percentage of their normal values and taking the mean. The TMI is thus made up of twelve different bilaterally performed muscle tests.

Reproducibility of TMI

TMI was estimated on five patients with RA who were measured for muscle strength threee times on three consecutive days. During this short time it was assumed that no major change in the clinical status of the patient would appear. The coefficient of variation was 0.58 per cent of the mean value indicating a very high reproducibility in the TMI calculations.

Abbreviated muscle index

Tornvall (1963) pointed out that "for practical reasons, muscle groups which are readily accessible for strength determinations and which show a high reproducibility are to be chosen". If also representativity for estimated general muscularity was taken into consideration, he recommended such tests as finger flexion, elbow flexion and knee extension for abbreviated muscle strength determinations. TMI estimations are very time-consuming and it would seem practical to use an abbreviated muscle index (AMI) when following the general muscle status of individual patients over periods of time. It must be noted, however, that the above recommended muscle tests for AMI estimations are applicable in healthy subjects. We do not know if they are so in patients with RA suffering from a disease with a marked tendency for spontaneous variations in local as well as systemic manifestations. It was assumed in this investigation, however, that if painless muscle contractions were used as far as possible, at least one important strength inhibiting factor, viz., joint pain that may bring about a rapid fall in the contractile force, was eliminated.

AMI consists of two tests performed bilaterally, viz., horizontal pull and knee extension. Horizontal pull combines the tests of finger flexion and elbow flexion recommended by Tornvall (1963) and also muscle groups surrounding the shoulder (m. latissimus dorsi and lower part of m. trapezius) take part. It is calculated in accordance with TMI calculations by adding the values of the individual tests expressed in percentage of their normal values and taking the mean. The AMI is thus made up of four different muscle tests.

Correlation between TMI and AMI

Simultaneously determined TMI and AMI in thirty-four patients with RA showed a correlation coefficient of $r = 0.94$. This indicates that AMI in this sample of rheumatic patients very closely reflects TMI.

Remaining methods used

Systemic disease activity was measured according to the methods outlined in Chapter 3 as ng ESR, orosomucoid content and α_2-globulin content in serum.

Table 14. *Clinical and laboratory data on 44 patients with RA*

Classification ...	"Classical" RA	"Definite" RA	"Classical" RA "Definite" RA
Number of cases	15	29	
Females	7	14	
Males	8	15	
Average age (years)			
Females			49.1
Males			56.7
Average duration of arthritis (years)			
Females	10.1	6.1	
Males	5.5	7.0	
Stage			
I	12	21	
II	2	6	
III	1	2	
IV	0	0	
Pos SSCA	15	16	

Statistical methods were the same as in Chapter 3. The degree of reproducibility for the TMI was determined by pooling together the individual coefficients of variation for the patient involved.

CLINICAL MATERIAL

The clinical material consists of thirty-four patients with RA treated at the Department of Rheumatology, Regionsjukhuset, Örebro from January 1968 until April 1969 and ten patients treated at Sätra Hälsobrunn during the summer of 1969. Most patients were in Steinbrocker stage I and II, a few, however, in stage III but fully capable of performing muscle tests.

Subjects

"Classical" RA: 15 patients, 7 females and 8 males. Rheumatoid progression according to Steinbrocker et al. (1949): 12 patients were in stage I, 2 in stage II, 1 in stage III and none in stage IV.

"Definite" RA: 29 patients, 14 females and 15 males. 21 patients were in stage I, 6 in stage II, 2 in stage III and none in stage IV.

The mean age in the female group was 49.1 years, in the male group, 56.7 years. The duration of the disease defined as the period of continuous joint symptoms ranged from 1 to 28 years. The average duration was 10.1 years for "classical" females, 6.1 years for "definite" females, 5.5 years for "classical" males and 7.0 years for "definite" males. Table 14 shows some clinical and laboratory data on forty-four patients with RA.

Table 15. *Range and mean values in percentage of normal values for different bilaterally performed muscle tests in thirty-four patients with RA.*

Muscle test	Range per cent of normal values		Mean	
	r	l	r	l
Gripping strength	9.2–100.0	22.1–108.0	52.0	54.2
Pinching	22.8–101.5	20.8–108.0	52.6	54.6
Pronation handle	21.7–113.7	28.6–133.2	63.8	64.6
Supination handle	9.6–114.3	25.8–148.3	59.2	61.7
Elbow extension	27.8–137.0	42.2–130.0	87.2	91.4
Elbow flexion	31.1–102.1	36.0–107.0	71.0	72.5
Horizontal pull	11.9–134.3	23.5–126.2	61.4	59.9
Horizontal push	13.8–178.0	23.4–196.0	74.5	79.0
Knee extension	42.8–111.5	41.2–130.0	77.5	82.4
Knee flexion	40.9–116.4	29.0–119.2	81.3	80.6
Plantar flexion ankle	37.9– 96.7	34.3– 89.9	60.0	58.6
Dorsal flexion ankle	47.7–132.0	44.4–137.9	79.0	79.2

Treatment

The patients received conventional antirheumatic therapy including salicylates, antiphlogistic agents, chloroquines, gold salts and steroids. In addition, they also received physical therapy and occupational therapy.

Methods of clinical and laboratory examination

Each patient was examined by the author according to the methods outlined in Chapter 1. In addition, the patients were examined for possible neurological symptoms, e.g., loss of tendon reflexes or sensory disturbances. No patient in the clinical material showed such symptoms. The patients at Sätra Hälsobrunn were not examined with X-rays but as a rule this had been done earlier. No test for rheumatoid factor was performed on these patients and they could therefore only be classified as "definite" RA although some of them might well have been "classical" cases.

RESULTS

Table 15 shows *the range and the mean values in percentage of normal values for different muscle tests in thirty-four patients with RA.* The mean TMI for the whole material was 69.1 per cent. A great variation was often found among the muscle test values within the single patient.

The relation between simultaneously obtained TMI and ESR values showed a correlation coefficient of r 0.46 (P 0.01). If the patients were divided into two groups according to the ESR, with the values 40 and 40 mm hour, respectively, a significant difference (t 2.88, P 0.01) was found between TMI

Table 16. *Results of AMI determinations for ten patients with RA treated at Sätra Hälsobrunn, 1969.*

The time interval between occasion I and II varied from 17 to 45 days. Simultaneous registration of ESR as a measure for systemic disease activity was effected.

Pat. no.	AMI I	AMI II	SR I	SR II	Time interval I–II (days)
1	23.2	24.5	82	75	30
2	29.4	38.9	51	33	45
3	30.8	38.9	117	72	17
4	39.8	40.2	57	50	18
5	36.5	44.3	33	43	45
6	22.8	27.4	54	44	18
7	34.0	34.4	38	43	38
8	39.2	47.0	42	57	28
9	44.3	30.7	36	48	24
10	23.2	29.8	58	43	30

values of the two groups, i.e., lower TMI values were accompanied by higher ESR values.

The relation between changes in AMI values and changes in systemic disease activity in twenty-three patients with RA simultaneously obtained at different occasions with intervals of about two months showed the following correlation coefficients:

r (diff. AMI; diff. ESR) $= -0.68$ ($P < 0.001$)

r (diff. AMI; diff. orosomucoid via acid electrophoresis) 0.77 ($P < 0.001$)

r (diff. AMI; diff. orosomucoid via gel electrophoresis) 0.60 ($P < 0.01$)

r (diff. AMI; diff. α_2-globulin) $= -0.59$ ($P < 0.01$)

These results indicate that, depending on which method for systemic disease activity that is used, changes in AMI are significantly or highly significantly related to changes in systemic disease activity on different occasions with about two-month intervals.

The effect of physical therapy (high repetition of movement against a submaximal load and intense progressive resistance exercises of upper and lower extremities three times a week) upon AMI was studied in ten patients at Sätra Hälsobrunn. The results are given in Table 16. The ESR was also registered in order to obtain some information about changes in systemic disease activity during the training period. In six patients there was an increase in AMI parallel to a decrease in ESR (cases nos 1 and 4 showed only negligible changes). In three patients, however, AMI increased while ESR also increased (slight changes in no. 7). Cases 5 and 8 indicate that in spite of increasing systemic disease activity intense muscle exercises in these two patients with RA resulted in increasing muscle strength. In one case ESR increased and AMI decreased in spite of muscle exercises.

COMMENTS

Physical therapy including assisted or active exercises progressing to resisted movement of joints is widely used at all stages of RA and is generally accepted as being necessary and helpful in the treatment program. This opinion is, however, mostly founded only on personal and general impressions. Little controlled worked on restoration of muscle strength in RA has been reported in the literature. Liberson (1961) demonstrated that brief isometric contractions are at least as valuable as isotonic exercises in the normal subject and in one case he also reported on a patient with RA. Machover & Sapecky (1966) showed an average gain of 23 per cent in the quadriceps muscle power in eleven patients with RA over a period of seven weeks using three maximum isometric contractions daily five days a week.

That muscle weakness is, in fact, a prominent feature in RA is indicated by the results of the present study. Great individual variations appear to be present among the patients and also in the muscle test values within the single patient. The range in single test values was impressive, especially as the contractions were considered painless by the participating patients. Especially gripping strength and pinching were often around 50 per cent of the normal values.

Calkins in a Committee report to the American Rheumatism Association Membership (1962) submitted semi-quantitative criteria for estimating degrees of disease activity in RA. These criteria were reviewed by Lansbury (1966). An ESR between 20 and 40 indicated "grade 1 activity group" while values between 41 and 70 indicated "grade 2 activity group". This division was used in the present study when comparing TMI values in patients with lower or higher systemic disease activity. It was interesting to find that, in spite of the fact that painful contractions were eliminated as far as possible, the difference in TMI values was significant (at the one per cent level) anyhow. This suggests that isometric contractions of rheumatoid muscles are influenced to a certain degree not only by the local disease process within the adjacent joint or within the muscle itself, but also by the systemic disease activity as such.

Moritz (1963) found no correlation between electromyographic changes in the intrinsic muscles of the hand and the ESR or the electrophoretic pattern of serum proteins. The involvement of these distal muscles was more closely related to the local arthritic process than to the general activity of the disease. The intrinsic muscles constitute proportionately small muscle volumes and it is hard to believe that the inflammatory process within them would influence systemic activity, at least not in cases of widespread joint involvement. In more bulky proximal muscles such as the brachial biceps and the quadriceps, he found no relation between the electromyographic changes and the presence of arthritis in neighbouring joints. Instead, the average value of gammaglobulin was

slightly higher in cases with an abnormal electromyogram in the brachial biceps. The precence of myopathy in this muscle was thus to a certain degree related to systemic disease manifestations. The incidence of myopathic changes was considerably lower (26 per cent) in proximal muscles (brachial biceps, deltoid, quadriceps) than in distal muscles of the hand (first interosseous, thenar), where, according to Moritz, changes were found in about 50 per cent of the patients.

Apparently, other factors besides pain and myopathy must contribute to muscle weakness as measured by means of TMI and AMI determinations. Systemic disease manifestations probably play an important role as suggested by the correlation between changes in AMI and changes in the different measurements of general activity found in this study. Engstedt & Strandberg (1966) reported a highly significant correlation between the hemoglobin concentration and the ESR and significant correlation between the hemoglobin concentration and α_2-globulin. It is tempting to speculate on the possibility that changes in the level of anaemia secondary to the clinical activity of the disease to some extent could influence the muscle strength values in RA.

Curtis & Pollard (1940) described focal round-cell infiltrations and an increase of interstitial nuclei in cases of RA. Since then several reports concerning muscle lesions in RA have appeared and Moritz (1963) gives a survey of the work in this field. Strandberg (1968) reported focal interstitial myositis as the most frequent lesion (39 per cent) in proximal muscles of cases with RA. Especially the acute form showed reactive cell infiltration with more or less pronounced inflammatory and degenerative histological changes, at times with perivascular oedema. Inflammatory changes are thus not only confined to the joint, but also present in the periarticular muscle tissue. Impaired vascularization in acute focal interstitial myositis provoking anaerobic metabolism of the fibroblasts and other cells may, perhaps, sometimes increase lactic acid concentration and lower the pH. Also proteolytic enzymes found in the lysosomes of connective tissue might liberate "acid" amio acids. Inflammatory reactions thus give rise to a local acidosis with increased glycolysis and increased hydrogen ion concentration which might explain the periarticular pain and muscle soreness (Menkin, 1956) found in cases of active RA. These factors ("metabolic myopathy") probably also influence muscle strength to some extent and might be reflected in the measurements of systemic disease activity used in this study.

When judging the effect of physical therapy, including active muscle exercises, favourable results might as well be due to decreasing systemic disease activity as to a real increase in muscle strength and it appears from a critical point of view also necessary to observe systemic activity during a training period.

CONCLUSION

Maximal voluntary isometric muscle strength determinations bilaterally in twelve different muscle groups in thirty-four patients with RA in Steinbrocker stages I–III have shown a mean muscle strength expressed as a total muscle index (TMI) of 69.1 per cent of the normal value found in healthy subjects. A significant difference in TMI (t 2.88, $P<0.01$) was found between patients with higher as compared to patients with lower systemic disease activity, i.e., the higher the activity is, the lower is the TMI. Abbreviated muscle index (AMI) determinations consisting of bilateral testing of two muscle functions (horizontal pull with the upper extremity and extension of knee) were closely correlated to TMI values of the patients. Changes in AMI values correlated to changes in the systemic disease activity, $P<0.001$ or $P<0.01$ depending on which method for systemic disease activity determinations was used. Physical therapy including intense progressive resistance or static muscle exercises during periods of between 17 and 45 days resulted in increasing AMI values in six of ten patients with RA. These observations were, however, also paralleled by a decrease in ESR. Three patients showed increasing AMI in spite of increasing ESR. It appears difficult to ascertain what caused the increase in AMI, muscle training or decreasing ESR. The material was very limited, however.

It is concluded that AMI estimations provide fast and simple general muscle strength determinations and could be used in studying variations in muscle weakness, a prominent symptom in all stages of RA.

Chapter 6

STUDIES ON FACTORS INFLUENCING QUADRICEPS STRENGTH IN RHEUMATIC KNEE JOINTS

Among factors besides pain that may restrict active contractions of different muscle groups in RA. are the presence of myositis (Petersén, 1955; Graudal & Hvid 1959; Strandberg, 1962; Moritz, 1963; Rossel, 1963) or effusion in the adjacent joint (deAndrade, Grant & Dixon, 1965).

Moritz reported that there was a connection between the appearance of abnormal electromyographic findings in the intrinsic muscles of the hand and the presence of active arthritis in MP joints and that the involvement of the intrinsic muscles was more closely related to the local arthritic process than to the general activity of the disease. The electromyogram was normalized during local remissions. Among proximal muscles the same relation was found between the deltoid muscle and the shoulder joint. No relation was found, however, between electromyographic findings in the quadriceps and the presence of active arthritis in the knee but the material was too small to permit any definite conclusions.

deAndrade et al. distended normal knee joints with plasma and observed a gradual weakening of the quadriceps before pain was experienced. In rheumatic knee joints pain preceded weakness of the quadriceps. Instillation of local anaesthetics delayed the appearance of weakness until the joint was distended at higher pressure. The studies suggested that stimuli from the knee joint cause reflex inhibition of the lower motor neurons supplying the quadriceps muscle.

Another restricting factor upon muscle strength in RA is atrophy arising from disuse, which may develop rapidly in acute phases of the disease but usually takes a long time to become generalized. The strength of the muscle is a function of the number and the diameters of the fibres in its physiological cross section and atrophied muscles contribute to muscle weakness. Quite normal electromyographic findings could be found, however, in severely atrophied muscles in RA (Moritz, 1963).

Reflex inhibition of the contraction of the quadriceps has been observed in response to other stimuli such as irritation due to injury (Swearingen & Dehne,

1964), and is a well known phenomenon in connection with knee surgery. Stener & Petersén (1962) showed that the vastus medialis undergoes reflex inhibition when pain receptors are stimulated in the medial collateral ligament of the knee joint and Stener (1969) has described reflex inhibition elicted from a subperiosteal tumour of the femur situated near the knee joint.

Various partly reversible factors apparently influence muscle contraction in RA. The aim of the following study was to obtain further information about the restricting effect upon isometric quadriceps strength caused by the local inflammatory process in the rheumatic knee joint and adjacent tissues, i.e., distal parts of the quadriceps muscle.

As far as possible, only painless muscle contractions were utilized in the calculations. The activity of the local joint disease process was graded with regard to the presence of active inflammation causing temperature elevation and with regard to the presence of effusion. The following problems have been studied:

1. Isometric quadriceps strength in relation to local knee joint disease activity.
2. Isometric quadriceps strength before and after removal of knee exudate.
3. Measurement of the intraarticular pressure in the knee joint with effusion.
4. Electromyographic findings in the quadriceps muscle on loading before and after removal of the knee joint exudate.
5. Single muscle fibre electromyography in the rheumatoid quadriceps muscle.

1. Material

Eighteen patients with "classical" or "definite" RA treated at the Department of Rheumatology, Regionsjukhuset, Örebro (RSÖ), 12 females and 6 males. Rheumatoid progression according to Steinbrocker et al. (1949): 11 patients were stage I and 7 in stage II. Mean age for females was 51.5 years and for males 45.6 years. Disease duration varied from 1 to 26 years. Ten patients were treated with steroids and eleven were seropositive with regard to rheumatoid factor. All patients had active knee inflammation with temperature elevation.

Methods

Isometric quadriceps strength was determined on two different occasions with about two months interval according to the method described in Chapter 5. Any palpable effusion in the knee was removed before the muscle test in order to avoid possible quadriceps inhibition due to increased intraarticular pressure. Local joint disease activity was measured using infrared thermography according to the method described in Chapter 1.

The same statistical methods as in Chapter 3 were used.

Table 17. *Heat counts and isometric quadriceps strength on two consecutive occasions with time intervals of about two months in eighteen out-patients with RA.*

Only knee joints with proportionately marked changes in heat emission were utilized. Corresponding changes in strength values varied from 1.8 to 47.0 percentage units. In Tornvall's material a variation coefficient in duplicate determinations of knee extension was around 4 per cent. In the report by Bäcklund & Nordgren quadriceps strength in two normal subjects recorded four times at intervals of one week showed a maximum deviation of about 4 per cent of the mean value.

Pat. no.	Heat counts arbitrary units			Muscle strength per cent of normal values		
	I	II	Difference	I	II	Difference
1	66	181	+115	61.4	53.1	− 8.3
2	221	4	−217	41.2	58.5	+17.3
3	212	150	− 62	77.5	96.5	+19.0
4	94	172	+ 78	71.0	54.6	−16.4
5	152	504	+352	94.2	66.8	−27.4
6	200	65	−135	85.5	112.1	+26.6
7	405	159	−246	37.8	82.0	+44.2
8	394	792	+398	86.3	64.1	−22.2
9	325	576	+251	68.9	52.7	−16.2
10	577	144	−433	56.0	81.1	+25.1
11	250	106	−144	86.0	133.0	+47.0
12	197	0	−197	70.0	98.6	+28.6
13	23	241	+218	68.1	54.3	−13.8
14	134	8	−126	88.8	108.0	+19.2
15	361	292	− 69	51.3	49.5	− 1.8
16	30	491	+461	60.7	47.1	−13.6
17	371	48	−323	44.4	66.0	+21.6
18	79	186	+107	50.6	33.7	−16.9

Results

Table 17 shows heat counts and quadriceps strength on two consecutive occasions in eighteen out-patients with RA treated under routine conditions using conventional antirheumatic therapy. Changes in quadriceps strength in this sample of rheumatic patients correlated to changes in local joint disease activity, $r = -0.84$.

2. Material

Ten patients with "classical" or "definite" RA treated at the Department of Rheumatology, RSÖ, 5 females and 5 males. Rheumatoid progression: 6 patients were in stage I and 4 in stage II. Disease duration varied from 1 to 25 years. All patients had palpable effusion in their knee joints.

Methods

Isometric quadriceps strength was determined according to the method earlier described in Chapter 5, before, immediately after and one day after aspiration

Table 18. *Quadriceps strength before, immediately after and one day after removal of different amounts of synovial fluid.*

Pat. no.	Joint	Quadriceps strength before aspiration (kpcm)	Amount fluid aspirated (ml)	Quadriceps strength immediately after aspiration (kpcm)	Quadriceps strength about 24 hours after aspiration (kpcm)
1	r k	1300	50	1300	1340
2	r k	420	10	400	420
	l k	1230	26	1270	1240
3	r k	1550	5	1500	1460
	l k	1480	30	1470	1500
4	l k	1080	83	1020	1110
5	l k	500	20	530	510
6	r k	900	50	880	900
7	l k	680	80	680	670
8	l k	830	15	850	870
9	r k	1030	32	1100	1140
10	r k	630	115	620	620

of the exudate using ordinary technique with sterile precautions without local anaesthetics. Joint puncture was performed just below the patella in order to avoid any possible damage to the quadriceps muscle. Two patients were measured bilaterally.

Results

Table 18 shows the quadriceps strength before, immediately after and one day after aspiration of different amounts of synovial fluid in twelve rheumatic knee joints. In none of the cases was the removal of exudate followed by any major immediate or delayed increase in the quadriceps strength.

3. Material

Four patients with RA belonging to the same patient group as in 2, one with "classical" and three with "definite" RA. Two patients were in stage I and two in stage II.

Methods

A 20-gauge needle was introduced into the knee joint cavity. As soon as fluid appeared in the needle it was connected via a polyethylene catheter to a strain-gauge pressure transducer model EMT 34 with a sensitivity range of 0–300 mm Hg. The intraarticular pressure was then recorded on a Mingograf model 81[1]. Pressures were obtained with the knee joint in different positions with the quadriceps relaxed or contracting. Usually the needle was introduced into the

[1] In collaboration with the Department of Clinical Physiology, Regionsjukhuset, Örebro.

Table 19. *Intraarticular pressures obtained in four rheumatic knee joints with different amounts of exudate in different positions with relaxed or contracting quadriceps muscle.* Pressures are given in mm Hg.

	Intraarticular pressures (mm Hg)			
Knee joint no.	1	2	3	4
Leg hanging straight	−1	63	—	—
Standing on leg	−2	89	—	—
Resting with straight leg	6	—	11	49
Quadriceps contracting with straight leg	248	—	318	—
Knee flexed 90 degrees	34	54	17	80
Knee flexed 90 degrees quadriceps contraction	—	378	57	—
Exudate aspirated	15	70	32	90

knee joint cavity from the lateral aspect at the level of the upper pole of the patella. Pain appeared, however, in one case when the knee was flexed to 90 during registration. A new puncture was then made from the frontal aspect below the patella lateral to the quadriceps tendon with the knee flexed 90 .

Results

Table 19 shows intraarticular pressures obtained in four rheumatic knee joints with different amounts of exudate in different positions with relaxed or tensed quadriceps muscle.

4. Material

Three patients with "definite" RA treated at the Department of Rheumatology, RSÖ, two in stage I and one in stage II with a disease duration of between 1 and 3 years. One patient was on steroid medication. Five knee joints were investigated.

Methods

Standard electromyographic technique was used in studying the quadriceps muscle. Recordings with concentric needle electrodes were made from different parts of the muscle. Surface electrodes (DISA bipolar) were placed symmetrically on the vastus medialis of the quadriceps muscle 10 cm proximal to the upper pole of the patella. The patient was sitting on a table with the knee in 135° flexion (Fig. 43). The EMG was recorded on a Revox tape recorder (type E 36) at rest and during submaximal loading with about 75 per cent of the maximal quadriceps strength measured according to the method described in Chapter 5. The load was produced by a weight around the ankle of the patient who was asked to keep his foot lifted with the knee remaining flexed at about

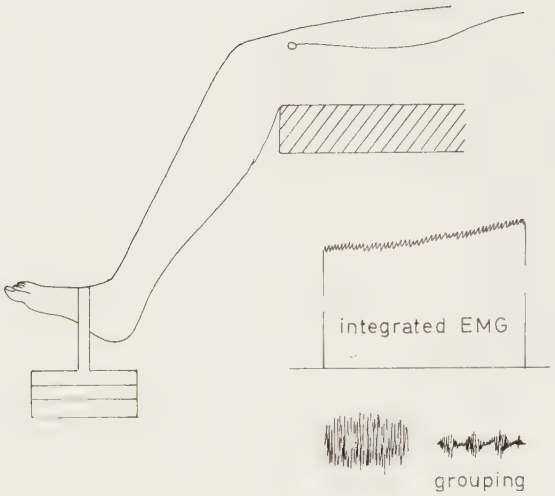


Fig. 43. During the EMG recordings using surface electrodes on the vastus medialis on submaximal loading the patient was sitting on a table with the knee in about 135° flexion.

135° as long as possible until exhaustion. EMG-recordings were made before and immediately after complete aspiration of the synovial fluid and were analyzed audiovisually (loudspeaker and memory oscilloscope) with respect to the shape and innervation frequency of the individual motor unit potentials and the interference pattern at maximal contraction. The signals were also integrated (R-C integrator with a time constant of 0.15 sec) and the results were recorded on an ink jet recorder.

Results

In all three patients the EMG-recordings showed slight myopathy-like changes in certain areas of the muscle. During submaximal loading the innervation frequency of the motor units remained largely the same before and after the aspiration of joint fluid. Amounts of removed fluid varied between 4 and 83 ml. The maximal force produced by the muscle did not change after the aspiration as judged from the isometric quadriceps strength determinations. Nor did the electromyographic findings regarding innervation frequency and action potential shape change after aspiration. However, there was a tendency toward increase in the integrated EMG during prolonged muscle work with grouping of the electrical activity occasionally into rythmic bursts. These electrophysiological signs of fatigue appeared after about the same period of quadriceps muscle contraction before and after joint fluid aspiration.

5. Material

Ten patients with "classical" or "definite" RA treated at the Department of Internal Medicine, Akademiska sjukhuset, Uppsala during 1965 and 1966 were

studied. Rheumatoid progression: 6 patients were in stage I, 2 in stage II, 2 in stage III. Mean age was 52.1 years. Disease duration varied between 2 and 23 years. Two patients were on steroids.

Methods

Single fibre electromyography was performed with a multielectrode according to the technique described by Stålberg (1966). The propagation velocity of the action potential from single muscle fibres was measured between two electrodes separated at a distance of about 200 μ in the multielectrode. About 10 muscle fibres in the quadriceps muscle on both sides from each of six patients were studied.

The neuro-muscular transmission was studied using the multielectrode according to the technique described by Ekstedt (1964) and Stålberg (1966) in about 10 to 20 motor end-plates in five to ten different sites in the quadriceps muscle of eight patients.

Results

Single fibre electromyographic determination of the propagation velocity in the sample of muscle fibres showed values varying from 2.5 to 4.5 meters per second which is within the normal range. Some patients were able to activate some of the motor units with a remarkably even frequency also at low mean frequencies, for example, 5.8 per second with a standard deviation of ± 0.19. At this frequency the variability expressed as standard deviation in normal muscles is usually more than ± 2.0 per second.

The neuro-muscular transmission, the "jitter-phenomenon" (Ekstedt, 1964), showed normal values. The variability in the transmission time in pairs of motor end-plates was between 10 and 35 μ sec expressed as standard deviation in all cases.

COMMENTS

The findings of a close relation between the painless maximum isometric quadriceps strength and the local knee joint disease activity indicate that inflammatory changes in the joint and perhaps also in the periarticular muscle tissue apparently constitute important factors among the different causes of muscle weakness in RA. Metabolic changes in connection with inflammatory reactions with increased carbohydrate utilization and glycolysis giving rise to local acidosis (Roberts, Mc Lees & Kerby, 1967) might explain the weakened muscle contraction through impaired muscle fibre function. When inflammatory activity subsides, muscle strength is restored to a certain degree. This "metabolic myopathy" thus seems to be partly reversible.

Moderate amounts of joint exudate did not influence the isometric strength

of the quadriceps. The intraarticular pressure registrations in the present study were made to provide further information about the pressure magnitudes seen in rheumatic knee joints with effusion in different positions with relaxed or tensed quadriceps. The results were in conformity with those obtained by Grant & Dixon (1963). Contrary to deAndrade et al. (1965), no further distension of the rheumatic knee joint until quadriceps weakening was performed. Neither before, immediately after, nor approx. twenty-four hours after joint fluid aspiration could any change in quadriceps strength or in the electromyographic findings on submaximal loading be observed. Ruffini-like receptors that respond to changes in capsular tension have been described in the knee joint of the cat (Skoglund, 1956). Stimulation of these receptors by increasing the intraarticular pressure caused an inhibition of the knee extensors and facilitation of the knee flexors in both the decerebrated and spinalized preparation (Ekholm, Eklund & Skoglund, 1960). If the neurophysiological adjustment to diminished intraarticular pressure would have taken some time it could have been expected that the quadriceps strength one day after the joint fluid aspiration would have increased. This was, however, not the case in this study. One explanation for this could be, as was shown by Haffajee, Moritz & Svantesson (1968), that only about 70 per cent of the motor units are activated at 10° flexion of the knee during maximum voluntary innervation. This angle was utilized in the experiments by deAndrade et al. Only minor inhibition due to increasing intraarticular pressure could at this flexion angle give rise to marked weakening of the quadriceps. At 90° flexion, at which angle quadriceps strength is determined using the technique in this study, maximum voluntary innervation activates a maximum number of motor units (Haffajee et al.). A minor reduction in the innervation at this degree of flexion was not enough to decrease quadriceps strength. In the experiments with surface electrodes on the vastus medialis during submaximal loading, the knee joint was kept at about 135° flexion where the quadriceps would exhibit maximum strength (Haffajee et al.). Not even at this position could an immediate change in the quadriceps strength be demonstrated after removal of the joint exudate. If joint effusion with increased intraarticular pressure through stretching of the ligaments and distension of the capsule would give rise to reflex inhibition of the quadriceps, the innervation frequency of the individual motor units should be low before and increase after aspiration. The low frequency before aspiration would need a higher number of motor units to perform the same muscle work as after the aspiration but the integrated EMG and the innervation frequency remained unchanged after removal of the joint exudate. Neither did the effusion influence the time to fatigue with the same load. The findings by deAndrade et al. (1965) are therefore not supported by the results in this study.

The weakness in the muscle could not possibly be ascribed to a generalized

muscle fibre atrophy as the propagation velocity, which is positively correlated to the fibre diameter, was within the normal range. The material was very limited, however. Neither could the weakness be explained by a disturbed neuromuscular transmission in individual motor end-plates as the "jitter-phenomenon" was normal in all end-plates studied.

CONCLUSION

A close correlation was found between the painless maximum isometric quadriceps strength and the local knee joint disease activity in eighteen patients with RA. No evidence of reflex inhibition of the quadriceps muscle due to knee joint exudate could be observed using isometric muscle strength determinations and electromyography with surface electrodes on the vastus medialis on submaximal loading. Single muscle fibre electromyography revealed normal propagation velocity in the muscle fibres and normal neuromuscular transmission in the motor end-plates of the rheumatoid muscle. The presence of a "metabolic myopathy" due to inflammatory changes in the muscle adjacent to active joints is suggested as a factor contributing to muscle weakness in RA.

GENERAL SUMMARY

The present investigation is a study of what information can be obtained about the clinical course of disease in patients with RA using some recently developed methods of evaluation. The interest has been focused on three common disease manifestations, viz., joint heat, joint stiffness and muscle weakness, all of which constitute parameters often used in evaluating schemes. The main problem in this investigation has not been to develop methods that can be used in antirheumatic drug trials. Instead, it was considered important to investigate the relation existing between the disease manifestations studied and to draw some general conclusions about their interaction within the rheumatic patient. Three methods have been applied, two objective and one semi-objective, viz., infrared thermography, visco-elastic joint stiffness registration in MP joints and maximal voluntary isometric muscle strength determinations.

In Chapter 1 infrared thermography and its application in the assessment of joint temperatures in RA is described. Quantitation of the thermogram has been especially discussed, a problem that must be taken into account if the method is to be used in clinico-rheumatological routine work. The importance of standardized measuring conditions is stressed. Quantitative methods based upon the use of isotherms and an infrared radiation reference source are suggested. In order to illustrate the use of thermal scanning in clinical practice it has been applied in studying the effect upon joint temperature as a measure of local inflammatory activity produced by some commonly used antirheumatic treatment principles.

In Chapter 2 an application of infrared thermography as a clinical method of estimating local joint disease activity is illustrated when comparing laboratory measurements of joint activity, i.e., white blood cell count and lactic dehydrogenase isoenzyme content in the synovial fluid. Similar changes occur in heat emission, white blood cell count and lactic dehydrogenase isoenzyme content during spontaneous fluctuations in local joint disease activity in nonsynovectomized knee joints with effusion. The changes in lactic dehydrogenase isoenzyme activity were, however, proportionately small.

In Chapter 3 the method for visco-elastic joint stiffness registration is described. It is confined to the second MP joints which, however, are often involved in RA. Elastic as well as viscous stiffness appear to be more closely correlated to local disease manifestations in the hand than to systemic disease activity. Cartilage destruction and joint space narrowing play only minor roles among

the factors contributing to joint stiffness, whereas active inflammatory changes in the joint such as capsular swelling and temperature elevation constitute important factors. Impaired muscular pumping action in the upper extremity with diminished venous return and incresed hand volume probably also give rise to increased primarily elastic stiffness. Morning stiffness, i.e., the difference between morning and afternoon values showed a close correlation with systemic disease activity, otherwise stiffness intensity values are not related to systemic activity. Tenosynovitis is accompanied by a marked increase in primarily viscous joint stiffness.

In Chapter 4 objective and subjective estimation of joint stiffness is compared in a group of rheumatic patients. Often there exists a discrepancy between objective clinical findings and subjectively experienced symptoms in RA and some patients tend to exaggerate the description of their complaints. Using psychological methods, the patients were tested with regard to intellectual capacity, neuroticism and introversion. It was found that the ability to describe stiffness intensity and morning stiffness duration in agreement with stiffness values obtained by means of objective registration and gripping strength determination (being an indirect measure of joint stiffness) was lower in patients that scored higher neuroticism values. IQ levels were lower in patients with a lower ability to describe unidirectional changes in subjective stiffness in agreement with objective registration and gripping strength determination. These results indicate that subjective joint stiffness estimations should be looked upon with caution in diagnostic and evaluative work in RA.

In Chapter 5 the method for maximal voluntary isometric muscle strength determination is described. Using this method in studying a clinical sample of patients with RA in stages I III, a general muscle strength of about 69 per cent of the normal value, expressed as a total muscle index comprising twelve different muscle tests bilaterally performed in the extremities, was found. Only painless muscle contractions, as far as possible, were utilized in the calculation. A significant difference on the one per cent level was found in general muscle strength when comparing two groups of patients with higher or lower systemic disease activity respectively. Changes in muscle strength correlated closely with changes in systemic disease activity. When judging the effect of muscle exercises in physical therapy for patients with RA the systemic disease activity should also be observed. A decrease in systemic activity is parallelled by increasing muscle strength.

In Chapter 6 isometric quadriceps strength is related to local knee joint disease manifestations such as temperature elevation and hydrops. Only painless quadriceps contractions were utilized in order to eliminate pain as a major inhibiting factor upon strength. Local joint disease activity by means of infrared thermography was closely related to quadriceps strength. Removal of knee joint

exudate was neither followed by an immediate, nor by a delayed increase in quadriceps strength. No evidence of a reflex quadriceps inhibition due to increased intraarticular pressure could be demonstrated using electromyography with surface electrodes on submaximal loading. Finally, a normal propagation velocity in the muscle fibre and normal neuromuscular transmission was found. The presence of a kind of "metabolic myopathy" contributing to muscle weakness in RA is discussed.

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